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THE BACKGROUND OF ANTIBIOTIC THERAPY IN SURGICAL INFECTIONS

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IT is not too much to say that at the present time at least half of all medical and surgical patients with infectious diseases receive antibiotic drugs as part of their treatment. The continued introduction of new drugs, with ever broader spectra or with increased specificity or potency, makes it imperative that there should be repeated critical evaluations of their logical place in the armamentarium, together with repeated critical evaluations of agents previously in use.

The purpose of this communication is to present the essential data concerning the antibiotics now in clinical use or under investigation, and to outline the general indications for their employment. The management of special clinical entities by antibiotic therapy is not part of the plan.

Bacterial or micro-organismal antagonism has been recognized since the early days of bacteriology, and the ability of various bacteria and fungi to produce antibacterial substances has been fully appreciated. Prior to 1938, however, these substances were considered at best as of limited usefulness and at worst as microbiological curiosities. Recognition of their important chemotherapeutic potentialities was limited and they were utilized chiefly for separating bacterial species from one another, which their selective action upon different bacteria made possible.

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Three investigations, in particular, established the basis for the recent advances in our knowledge of antibiotics. They dealt, respectively, with the bacteria, the fungi, and the actinomycetes, that is, with the three groups of micro-organisms now considered the most important producers of antibiotic substances.

1. The work of Dubos in 1939 (15) concerned the tyrothricin complex produced by the Bacillus brevis. His investigations not only served to focus attention upon the important group of antibiotics which are polypeptides in nature but laid the foundation also for extensive studies of aerobic spore-bearing bacteria. These studies resulted in the isolation of a large number of compounds, including, among many others, subtilin, bacitracin, and polymyxin.

2. The work of the Oxford group, headed by Abraham and Chain (1, 2), concerned penicillin (1940–1941). The original studies were followed by numerous others on penicillin-producing fungi and other fungi capable of producing antibiotics. The later studies resulted in the isolation of a large number of antibiotic substances, of which only the penicillins have thus far shown any outstanding promise as chemotherapeutic agents.

3. The investigations of Waksman and his associates in 1940–1942 (60, 72, 73, 75, 76) concerned antibiotics produced by actinomycetes. These studies, which resulted in the discovery of streptomycin, were followed by numerous others which resulted in the isolation of a large number

of other antibiotics. Among these, aureomycin and chloromycetin, and, more recently, terramycin, have been established as effective therapeutic drugs.

During the last 6 years the major role in the treatment of infections, once held by the sulfonamides, has been given over to the antibiotics, especially to penicillin. Penicillin has been found to accomplish all that the sulfonamides can accomplish against gram-positive bacterial infections, and to attain these results without their toxic manifestations. This agent, however, is not potent against most gram-negative organisms, nor against mycobacterial, rickettsial, viral, protozoal, and fungal infections. Moreover, it has not been as effective in controlling mixed infections as it has been in monobacterial infections, principally because certain bacteria have the power of producing an enzyme, penicillinase, which inactivates it.

In spite of these limitations, as penicillin has become more available and less expensive, physicians have become more and more prone to use it indiscriminately, without trying to ascertain either the nature of the organism causing the infection or its possible susceptibility. As a result, there have been a distressing percentage of therapeutic failures and a consequent delay in resorting to appropriate treatment. Some physicians, in order to offset these failures, have employed larger and larger dosages for indefinite periods, even when it was obvious that this antibiotic was of little or no value in the particular case. If penicillin were a panacea, or if it were the only antibiotic at our command, there might be some justification for using it in the treatment of every case of infection and awaiting the result of therapy without attempting to determine the cause of the disease. Since effective alternative measures are available, this course of action is as ill-advised as it is illogical. The physician now has the choice of streptomycin, bacitracin, aureomycin, chloromycetin, terramycin, and polymyxin, all able to control types of infection which are known to be refractory to penicillin, and he is not giving his patient the best he has to offer if he does not use the most specific and most potent of these drugs when they are indicated.

To be acceptable as a therapeutic agent, an antibiotic should possess certain positive and negative characteristics.

The ideal antibiotic would:

1. Be inhibitory in vivo at concentrations which do not injure the host.
2. Reach the pathogens in any location.
3. Be easy to administer.
4. Be cheap.
5. Be stable for storage.

The ideal antibiotic would not:

1. Impair antibody or phagocytic activity.
2. Be rendered ineffective by mutations (resistance).
3. Antagonize the effects of other agents.
4. Have toxic effects.

All these criteria are important, but in the determination of which antibiotic is best suited for a specific disease entity, the absolute minimal data required are (1) its effectiveness, (2) its relative toxicity, (3) the ease with which it can be given, and (4) the cost to the patient. The latter consideration, which for practical reasons cannot be ignored, includes not only the cost of the drug per se but also such concealed charges as hospitalization, syringes, needles, and supplemental drugs.

PENICILLIN

Penicillin, which represents the most important single advance in our therapeutic armamentarium against infections, was discovered in 1928 by Fleming, was first produced in concentrated form by Chain and the Floreys in 1940, was first made available in the Army in amounts sufficient to conduct limited clinical trials late in 1942 (40), and was first made available to the medical profession in 1944. It is a clinical weapon of unsurpassed excellence, chiefly because it is the only antibiotic with negligible toxicity at doses of even a thousand times those required for minimal therapeutic effect.

Chemically, penicillin appears to be a ring condensation of two amino acids, alanine and beta-dimethyl cysteine (11, 20). Various penicillins have been shown to differ in the substituent acid coupled to the alanine-amino group. Synthesis by the mold Penicillin notatum is still more efficient than laboratory chemical production.

Properties. The penicillins are moderately strong acids, whose potassium, sodium, calcium, and other salts can be employed therapeutically. The acid penicillin will react with the base procaine to form a salt known as procaine penicillin, which is relatively insoluble. This property is the basis of a new principle of penicillin administration because, as a result of its low solubility, a repository injection of a suspension of this salt results in delayed absorption and prolonged blood concentrations.

Penicillin G, benzyl penicillin, the most commonly used form of penicillin, is now available as the potassium or sodium salt in pure crystalline form and is of standard potency (1 milligram =

1667 Oxford, antistaphylococcal, units). It requires no refrigeration unless it is diluted. The procaine salt is stable and need not be refrigerated. Procaine penicillin G is compatible with sulfadiazine but not with sulfanilamide.

With certain exceptions, penicillin has a marked selective affinity for gram-positive organisms and spirochetes. The Mycobacterium tuberculosis and Streptococcus faecalis are not susceptible; conversely, gram-negative cocci, such as Neisseria gonorrhoeae and Neisseria intracellularis, are highly sensitive. Penicillin also is effective in vivo against the two large viruses that cause psittacosis and ornithosis.

Penicillin is bacteriostatic in threshold concentration and bactericidal in higher concentration. Its bacteriostatic action precedes its bactericidal action. The onset of bacteriostasis, which is preceded by a short lag period, is observed only on actively growing bacteria. Organisms which are at rest or which are not reproducing are unaffected. Bacteria exposed to penicillin show morphologic abnormalities, notably in those forms that fail to divide. Recovery of these damaged cells requires a favorable environment, and 3 to 8 hours may ensue before multiplication takes place, the time depending on the concentration of penicillin to which they have been exposed and the duration of exposure. During the period of exposure, bacteria are highly susceptible to the defense mechanisms of the body. This phenomenon explains why the therapeutic effect of penicillin in vivo is greater than in vitro and why it persists for many hours after the drug has fallen to ineffective concentrations.

The activity of penicillin is greatest at *p*H 6 to 6.5. Strong acids or alkalies cause it to decompose. Oxidizing agents and cysteine inactivate it. Its activity is maintained in the presence of blood, serum, pus, and large numbers of bacteria. In therapeutic concentration penicillin does not injure leucocytes or tissues.

The problem of how penicillin acts, as well as why it acts more effectively on gram-positive than on gram-negative bacteria, is still largely unsolved. The factors which chiefly influence its antibacterial action include:

1. Strain sensitivity. Not all gram-positive bacteria of any genus are susceptible to penicillin. Resistance (both natural and acquired) is most commonly encountered in the Staphylococcus and nonhemolytic Streptococcus species and least often in Neisseria organisms.

2. Penicillinase. This enzyme, which is produced by some bacteria, notably those of fecal and soil origin, inhibits the antibacterial action of penicillin, and explains some, but not all, of the types of bacterial resistance encountered clinically (1). In the laboratory, the incorporation of penicillinase into bacterial mediums to neutralize the penicillin present in the body fluids is of value, 1 unit per cubic centimeter of body fluids usually being employed.

3. The action of penicillin on bacteria. Gale and Rodwell suggest that penicillin exerts a direct effect upon nucleic acid metabolism within the growing cell, which possibly impairs its power to assimilate amino acids. Organisms resistant to penicillin have the ability to grow and reproduce without assimilating and concentrating glutamic acid, and thus, by an alternate metabolic pathway, become independent of the penicillin action. These observations suggest that penicillin owes its high chemotherapeutic ratio to a specific interference with metabolism that is not shared to any important degree by most tissues which divide rapidly.

Drug levels. Over the past 2 years there has been accumulating evidence to suggest that the maintenance of a more or less constant blood level of penicillin is unnecessary for efficient treatment of human beings with penicillin-susceptible infections (41). There are several explanations for this trend in chemotherapeutics:

1. As already noted, organisms exposed to static concentrations of penicillin cease multiplying and are damaged to the extent that they do not resume normal growth for several hours after drug therapy has been discontinued. The duration of the postpenicillin recovery period varies from strain to strain, with the concentration of penicillin used, and with the duration of exposure (19). The recovering bacteria which have been damaged, but not killed, by the drug are remarkably susceptible to the host defences. In effect, the bactericidal process in vivo continues for many hours after the drug itself has fallen to inhibitory concentrations (18).

2. The time required for bacteriostasis to become manifest varies with the concentration of drug to which the organisms are exposed as well as with the types of organisms to be affected. With some strains of streptococci and pneumococci the bacteriostatic effects take place within 45 minutes after contact with the drug. Other organisms, such as Treponema pallida, may not be affected for 24 hours (18).

3. The selective accumulation of penicillin in inflamed tissue is an important factor in the therapeutic effectiveness of single or twice daily doses of the drug. After the intramuscular injection of penicillin, detectable amounts remain

trapped in the fluid of damaged or inflammatory tissue approximately twice as long as in the blood stream, the drug diffusing out of tissue as the concentration in the blood plasma falls (68).

The principal characteristics of penicillin are its poor absorption by mouth, its rapid absorption from intramuscular depots, and its extremely rapid renal excretion, which results in fluctuating levels with high peaks and deep valleys. Excretion is largely via the urine. Significantly, penicillin is a highly soluble substance which diffuses rapidly throughout the body, and which, after a single parenteral injection, can be obtained from, and identified in, all body tissues with the exception of the brain, nervous tissue, and fat. It diffuses into the ocular tissues, slightly into the spinal fluid in the presence of meningitis, and, when very large doses are used, into the infected joint fluid and into pleural fluid.

Establishment and maintenance of blood levels depend upon the following factors: dosage and frequency of administration; rate of absorption from the drug depot; rate of drug inactivation in the body; degree of binding to plasma and other tissue proteins; and rate of excretion.

After a single intramuscular or intravenous injection of 100,000 units of penicillin, the blood serum level rises to 0.6 or 0.7 units per cubic centimeter in the first 15 minutes (18). This level is halved in the next 15 minutes and halved again in the following 15 minutes. After 1 hour the level is in the vicinity of 0.07 units, which is maintained for about 2½ hours.

When penicillin is injected intramuscularly in a volume of 1 or 2 cubic centimeters, 300,000 units provide a therapeutic level in excess of 4 hours. A million units provide a therapeutic level for approximately 8 hours. When, therefore, it is given at either 8 or 12 hour intervals, plain aqueous penicillin provides adequate treatment in the majority of the common infections (67).

A single 300,000 unit intramuscular injection of procaine penicillin G suspended in 1 cubic centimeter of water or oil is, because of its low solubility in the body fluid, released much more slowly and provides penicillin levels in the blood plasma for 18 hours or longer (30). In our own experience (54), a plasma level of 0.05 units is provided for at least 18 hours in all patients. Urine levels in excess of 200 units for 12 hours are usual, followed by a gradual elimination from the body for 36 hours. The advantages of procaine penicillin are high blood levels for a long period, reduction in the number of injections required, absence of discomfort at the site of injection (a decided advantage in the treatment of infants and children), few side effects at the site of injection, and its stability for long periods at room temperature. It should be emphasized that this product is suitable only for intramuscular injection.

In a recent study (28) in which two groups of patients with similar infections were treated, respectively, with injections of 300,000 units of procaine penicillin G in oil and with twice daily injections of 300,000 units of aqueous penicillin G, no significant difference in response was observed.

Penicillin is being used with increasing frequency by the oral route. Three to five times the usual intramuscular dose yields blood serum levels of comparable magnitude. The belief that gastric acidity was largely responsible for inactivation of the drug when this route was used has been generally discarded for lack of evidence. Actually, most of the penicillin given is absorbed in the upper part of the small intestine and its destruction by penicillinase in the upper digestive tract is negligible (66). The most important factor influencing gastrointestinal absorption seems to be an inherent individual variation in the absorptive capacity of the gut. Experience has shown that absorption is irregular and unpredictable unless the dosage in adults exceeds 250,000 units (31). On the positive side, use of the oral route eliminates the expense of sterile equipment required for injection and the discomfort attending injections. Methods of improving the absorption of penicillin are under intensive investigation at this time.

In the treatment of localized infections by penicillin much may be gained from the achievement of a local drug level higher than can be obtained following parenteral administration (44). This principle is applied in infections of the skin, oral and other mucous membranes, paranasal sinuses, pleura, joint spaces, open wounds, and abscess cavities. Aqueous penicillin G is employed for this purpose (35). Surface infections respond to 500 to 5,000 units per milliliter in an appropriate vehicle. In intrapleural infection, after aspiration of the pleural cavity, 50,000 units or more of penicillin dissolved in 500 cubic centimeters of saline solution are injected. In acute septic arthritis, 4 to 5 cubic centimeters of penicillin, containing 10,000 units or more, are instilled directly into the joint space after it has been aspirated. Penicillin may be used intrathecally in the treatment of meningitis in a maximal dose of 10,000 units. It is useful by nebulization in certain infections of the respiratory tract and can be administered preoperatively by this route as prophy-

laxis against infection. Twenty thousand units per milliliter are employed customarily.

STREPTOMYCIN

Streptomycin, a metabolic product of Streptomyces griseus (a soil actinomyces), is a colorless crystalline salt, which was first isolated in 1944 by Schatz, Bugie, and Waksman (60, 76). It owes its position as a therapeutic agent alongside penicillin to its preferential activity against gram-negative and acid-fast organisms. The activity of streptomycin against staphylococci and streptococci overlaps that of penicillin, aureomycin, and chloromycetin. It overlaps with sulfadiazine, aureomycin, and chloromycetin against some gram-negative bacilli and with viomycin, neomycin, mycomycin, p-aminosalicylic acid, and thiosemicarbazone against tubercle bacilli.

Structurally, streptomycin is a glycoside (47). Its antibacterial activity is lost once it is hydrolyzed. It is commercially available as a freely soluble trihydrochloride, calcium chloride double salt, or sulfate, and is usually administered as such. Streptomycin salts are stable at room temperature over long periods of time, for which reason refrigeration is unnecessary. Solutions are stable at *pH* 3 to 7 for at least 60 days.

Mode of action (73). The exact mechanism of the antibacterial action of streptomycin, like that of penicillin, is unknown, but certain established factors bear on its mode of action:

1. Its activity varies directly with its concentration, i.e., the rate of killing of bacteria steadily increases as its concentration is increased. This observation points to the desirability of obtaining relatively high concentrations in the body. The larger the size of the inoculum, the greater the concentration of streptomycin required to inhibit microbial multiplication completely.

2. The activity of the drug is greatest in an alkaline, and least in an acid, environment.

3. The action of streptomycin is antagonized by concentrations of organic and inorganic salts in the environment and by many sulfhydryl compounds, including cysteine.

4. Like most other antibacterial agents, streptomycin has both a bacteriostatic and a bactericidal action.

5. Streptomycin, like penicillin, produces an alteration in bacterial morphology coincident with bacteriostasis.

It is thus apparent that a definite conclusion concerning the mode of action of streptomycin cannot be reached at present.

Drug levels. To ensure adequate serum and tissue levels of streptomycin, parenteral administration is necessary. The usual parenteral dose is 1 to 3 grams a day in two or four divided doses. After an infection the drug is found to be distributed throughout extracellular fluids. With usual doses the values obtained in the blood, following a single intramuscular injection of streptomycin, are related to the dose per unit of body weight. In 4.0 to 20.0 milligrams per kilogram doses, the rate of fall in serum concentrations is proportional to the rate of renal clearance of the drug. The rate is not rapid, approximately 2½ hours being required for the concentration to fall from any given value to half the value. For this reason intervals between doses of 6 to 8 hours, or even longer, prove generally satisfactory. Streptomycin passes readily from the blood serum into the peritoneum and diffuses even more readily into the pleural fluid. Diffusion into the cerebrospinal fluid does not occur readily in the absence of meningitis and, even in the presence of this disease, the administration of streptomycin may fail to produce therapeutically significant levels. For this reason, intrathecal administration may be necessary. The maximal intrathecal dose is from 1 to 1.25 milligrams per kilogram per day. Absorption from the spinal fluid into the blood is as poor as in passage in the reverse direction.

Streptomycin, in contrast to penicillin, is unabsorbed by the oral route, although it is not destroyed in the gastrointestinal tract. This convenient route for systemic therapy is, therefore, barred; however, its employment against enteric pathogens is possible. Very large doses may be given by mouth for intestinal disease (Shigella infection) caused by gram-negative bacteria.

Streptomycin is administered frequently by inhalation (nebulization), and high concentrations are found in the sputum. The maximal dose, which is the same for topical application, is 100 milligrams per cubic centimeter per day.

Streptomycin is excreted chiefly by renal glomerular filtration without tubular reabsorption or secretion. A small amount is excreted in the intestine and in the bile. No clear evidence exists to indicate metabolism of the antibiotic in the body.

DIHYDROSTREPTOMYCIN

Dihydrostreptomycin, which is produced by the catalytic hydrogenation of the parent compound, was introduced in 1948 as a potentially less neurotoxic agent. The report of the Council on Pharmacy and Chemistry of the American Medical Association of 1950 (57) summarizes the status of this antibiotic as follows:

"*Actions and uses.* Dihydrostreptomycin shares the actions and uses of its parent compound,

streptomycin. Like streptomycin, it is effective against a variety of gram-negative and gram-positive pathogenic bacteria, including the tubercle bacillus, and to a lesser extent against infections due to Pseudomonas aeruginosa or Proteus vulgaris. The common predisposition for the development of resistance of the infecting organisms to streptomycin applies with equal emphasis to dihydrostreptomycin. It may be used in the following conditions: subacute bacterial endocarditis (in staphylococcic or streptococcic infections only when penicillin-resistant or streptomycin-sensitive); acute gonorrhea (penicillin-resistant); urinary tract infection due to susceptible gram-negative bacilli; and peritonitis due to gram-negative bacilli. It is also used for prophylaxis in surgery of the gastrointestinal tract and intrathecal infection in tuberculous meningitis. In brucellosis dihydrostreptomycin may be used in combination with sulfadiazine if aureomycin and chloromycetin are not available.

"Like streptomycin, dihydrostreptomycin is capable of producing neurotoxic manifestations such as vestibular and auditory dysfunction.

"Audiometric tests for vestibular function should be made prior to prolonged treatment with the drug and thereafter repeated at least every two weeks during therapy. Skin or allergic reactions occur as with streptomycin. If these reactions are mild, they may be controlled with histamine-antagonizing agents; if they persist, it may be necessary to discontinue the drug or change to streptomycin. When toxic reaction occurs, clinical judgment must be exercised as to termination of therapy. During treatment with dihydrostreptomycin it is advisable to carry out periodic in vitro tests to determine sensitivity of the causative organism to various antibiotics.

"*Dosage.* Dihydrostreptomycin is administered as the hydrochloride or sulfate in doses similar to those of streptomycin. Unlike streptomycin, dihydrostreptomycin must be injected by the intramuscular route only. *It must not be injected intravenously.* The sulfate may be given by the intrathecal route in doses not to exceed 1 mgm. per pound of body weight up to 50 pounds of weight. It may be given daily or on alternate days. Intraspinal therapy is rarely indicated in any condition other than tuberculous meningitis.

"Intramuscular injection of the drug may cause pain, which may be reduced by observance of the following suggestions: (a) allow 12-hour intervals between injections; (b) use only fresh solutions; (c) restrict maximum volume of injection at any one site to 2 cubic centimeters; (d) use the upper outer quadrant of the buttocks and change site for each injection; (e) insert needle deeply to avoid subcutaneous deposition and inject slowly; (f) as the diluent, use a local anesthetic with distilled water; (g) avoid concentrations whose dihydrostreptomycin base equivalent is greater than 500 milligrams per cubic centimeter of solvent. Each 500 milligram equivalent of the powder contributes approximately 0.3 cubic centimeter to the volume of solution made."

AUREOMYCIN

Aureomycin, which was described by Duggar (17) in 1948, is elaborated by a new species of the actinomycetes, named by him "Streptomyces aureofaciens." Preliminary tests indicated that aureomycin was active against a wide bacterial spectrum as well as against rickettsia. Duggar's coworkers at the Lederle Research Laboratories crystallized aureomycin. Although its structural formula has not yet been definitely established, this antibiotic is known to be a weakly basic compound which contains both nitrogen and nonionic chlorine. The hydrochloride has a solubility of 14 milligrams per milliliter at 25 degrees centigrade, and in solution has a *p*H of 2.9

The drug is supplied in 250 milligram capsules for oral administration, and in vials, in 100 milligram amounts, with sodium glycinate, for intravenous use. Crystalline aureomycin hydrochloride is stable in the dry state and will maintain its potency for several months at cool room temperatures. Solutions are potent for only a short period of time even when refrigerated. The drug becomes quite unstable at a neutral or alkaline *p*H, even at 4 degrees centigrade, and its instability increases progressively as the temperature is raised.

Aureomycin has a wider range of activity than either penicillin or streptomycin. It is effective against numerous gram-positive and gram-negative bacteria, all species of pathogenic rickettsia, and possibly several viral agents and protozoa. It is less bacteriostatic in alkaline than in acid media, which is the reverse of streptomycin. Differences in the size of the inoculum have a moderate effect upon the minimal threshold concentration.

The bacteriostatic properties of aureomycin are also adversely affected by meat infusion, peptones, yeast extract, blood, fresh or heat-inactivated serum, and phosphate buffer. The variation between the bacteriostatic and bactericidal end points in vitro is marked.

Gram-positive cocci and bacilli are somewhat less sensitive to aureomycin than to penicillin, but several clostridial species by and large are equally

susceptible to both drugs (9). Some strains of Streptococcus faecalis are more sensitive to aureomycin than to penicillin. Most gram-positive organisms and the gram-negative Brucella and Neisseria are inhibited by 1 microgram or less per milliliter. Treponema pallida and other spirochetes are highly sensitive to aureomycin. Gram-negative bacilli require somewhat higher concentrations of aureomycin, their requirements ranging from 3.1 to 25 micrograms per milliliter.

Aureomycin was promptly found to be curative in rickettsial infections in both animals and chick embryos, although there was no direct effect upon these organisms in vitro (58). Just how much antiviral activity it exhibits is conjectural. It has amebicidal activity in vitro. Unfortunately, the majority of strains of Proteus and Pseudomonas aeruginosa are moderately to materially resistant. Aureomycin is tuberculostatic in vitro but lacks this therapeutic effect in vivo.

It is of considerable interest and importance that many penicillin-resistant organisms are susceptible to aureomycin, as are streptomycin-resistant organisms (except the Proteus and Pseudomonas). Also of importance is the demonstration that resistance to aureomycin is seldom developed by bacteria. In this respect aureomycin resembles penicillin. The mode of action of the drug is not understood at this time. Bacteria do not elaborate an enzyme capable of destroying aureomycin.

Aureomycin, as has been pointed out, is rather unstable in serum and body fluids, and this property has handicapped workers who were studying its absorption and excretion. For this reason it is advisable to store samples for assay at once in the frozen state until the time for actual testing. The observation that aureomycin deteriorates less readily in thioglycollate broth than in other media now permits assay of fluid by the serial tube dilution test and also permits incubation overnight (29).

Drug levels. Intramuscular injection is painful and impracticable. Oral administration is the method of choice. From 2 to 4 grams daily are now regarded as the standard dose in acutely ill adults, 0.50 to 1 gram being given at intervals of 6 hours. For children the recommended dose is 250 or 500 milligrams every 6 hours, given with jam, jelly, or other foodstuffs. Following the oral administration in man of single doses of 0.75 to 1 gram, aureomycin is readily absorbed into the circulation and a maximal concentration of 4 micrograms per milliliter is usually reached and maintained at a constant level for several hours. Repeated prolonged administration at 6 or 8 hour intervals does not result in concentrations higher than 8 micrograms per milliliter, which suggests that there is no "piling up" effect in the absence of impaired renal function.

The use of aluminum hydroxide, to reduce aureomycin-induced gastrointestinal distress, nausea, and vomiting, is contraindicated, since the gel appears to interfere materially with the absorption of aureomycin and therefore with its therapeutic effectiveness (70). On occasion, reduction of the dose by one-half for a short period may lessen gastrointestinal irritation. Because of the powerful suppressive effects of aureomycin on fecal flora, vitamin supplements should be given when it is to be administered for more than 7 to 10 days.

Intravenous injection of the drug with sodium glycinate is feasible but should be reserved for the patient unable to take the drug by mouth. The intravenous dose is usually one-quarter that of the oral dose. Five-tenths gram dissolved in 250 cubic centimeters of saline solution, delivered through an 18 gauge needle over 15 to 30 minutes, may be given every 12 hours. The veins of the upper extremity should be used whenever possible. Because repeated injections may result in thrombophlebitis, intravenous therapy should not be used over an extended period of time.

Intravenous administration of 0.5 gram of aureomycin in 250 cubic centimeters of saline solution by gravity flow produces therapeutic blood concentrations (2 to 4 micrograms per milliliter) 12 hours after injection. Maximal doses of from 4 to 16 micrograms per milliliter are obtained at 3 hours and are halved at 6 hours. Traces of the drug may persist in the blood for 24 hours. Dissemination through the circulation is general, and antibacterial amounts have been demonstrated in many body fluids and tissues. In contradistinction to penicillin and streptomycin, aureomycin traverses the blood-brain barrier and diffuses readily into the cerebrospinal fluid in amounts which are considered therapeutically effective. It is, therefore, a useful agent in the treatment of infections of the central nervous system. It diffuses through the placenta and is available in the fetal circulation. When therapeutically effective amounts are present in the blood, diffusion into the pleural fluid occurs. Because of its locally irritating properties, aureomycin should not be used intrathecally, intrapleurally, or by nebulization.

Aureomycin has been found in the liver, bile, kidney, spleen, and lung (29). Large amounts are excreted in the urine after oral administration, sometimes for 2 or 3 days after its withdrawal. The drug is also excreted in the intestinal tract

during passage through which it is remarkably effective in suppressing or eliminating sensitive bacteria.

CHLORAMPHENICOL (CHLOROMYCETIN)

In 1947 Burkholder demonstrated the antibiotic activity of extracts from a soil actinomycete, Streptomyces venezuelae. Soon afterward, Ehrlich and Bartz of Parke-Davis Research Laboratories announced preparation of the material in crystalline form (21, 22). Smadel and Jackson, at the Army Medical Department Research and Graduate School, demonstrated its powerful activity against experimental rickettsial and large viral infections (63). Other biologic studies followed rapidly. In 1949 Controulis, Rebstock, and Brooks synthesized the material. The structural formula is D-(threo)-1-p-nitrophenyl-2-dichloroacetamido-1, 3-propanediol.

The natural and the synthetic forms of chloromycetin are identical in chemical, physical, and clinical properties. The drug is a white crystalline substance with a bitter taste, and a neutral reaction which differentiates it from aureomycin. It is stable in neutral and acid solutions for more than 24 hours, and is unaffected by boiling in distilled water after more than 5 hours. Its solubility in water at room temperature is low, but it is soluble up to 15 per cent in propylene glycol.

The drug is supplied for clinical use in 250 milligram capsules for oral administration. Since the pure crystalline material is available, no bioassay is needed and dosage is in terms of weight only. Bioassay in experimental animals and men may be estimated by the turbidimetric method, based on suppression of growth of the Shigella paradysenteriae. The threshold of sensitivity of the method is 1 microgram of chloromycetin per milliliter.

Like aureomycin, chloromycetin exerts a bacteriostatic, not a bactericidal, effect. It is highly bacteriostatic against the pathogenic rickettsia, and antiviral against the viruses of the psittacosis lymphogranuloma group. The antibacterial spectrum is qualitatively the same as for aureomycin (9, 43): streptococci, pneumococci, staphylococci, anthrax and diphtheria bacilli, and the actinomycetes, Actinomyces bovis and Nocardia asteroides, are, in general, slightly less sensitive to chloromycetin in vitro than to aureomycin, and considerably less sensitive than to penicillin. The antispirochetal activity of chloromycetin is of low order. It is about one-tenth as active as is streptomycin against Mycobacterium tuberculosis, and in vivo tests have not been encouraging. Most gram-negative bacteria are inhibited by concentrations easily obtainable in the blood (less than 10 micrograms per milliliter. Many strains of the Proteus are susceptible to chloromycetin, while the Pseudomonas is generally refractory.

With both chloromycetin and aureomycin, considerable variation is encountered between genera as well as between species, and even between strains within species. Attempts to induce increased resistance to chloromycetin have been successful in the instance of some bacteria, but not for rickettsia in the embryonated egg. Development of resistance of certain gram-negative bacteria as a cause of failure in the therapy of human infections has been reported (5, 27). As with aureomycin, chloromycetin resistance of bacteria should not be of major clinical significance.

The mechanism of action of chloromycetin on micro-organisms is not known. The drug does not inhibit several of the intact enzymes present in bacterial cells, nor does it block the phenolic hydroxyl groups, amino groups, carboxyl groups, or the sulfhydryl groups in the proteolytic enzymes tested, which are necessary for enzymatic activity. It is broken down partially by the action of enzymes liberated into the culture medium by the intact Proteus vulgaris, Bacillus subtilis, Bacillus mycoides and Escherichia coli. The enzymes, which appear to be related to the papain group, act on chloromycetin by hydrolysis of the amide linkage (64).

The antirickettsial and antiviral activity of chloromycetin and its action against experimentally produced gram-negative infection have been established.

Drug levels. Chloromycetin is stable in serum and body fluids. The material is absorbed readily from the gastrointestinal tract, and blood serum concentrations reach a peak within 2 hours after a single dose. A small amount is still measurable at 8 hours (61). Maximum serum concentrations tend to be proportional to the dose administered. When a 2 gm. dose is administered to man, blood levels of from 15 to 30 micrograms per milliliter have been found at 30 minutes, half this level at 2 hours, and about 5 micrograms per milliliter at 8 hours. Like aureomycin, chloromycetin diffuses into the cerebrospinal fluid. The concentration of drug in the spinal fluid, bile, and milk of human beings is about half that found in the blood.

Chloromycetin is excreted largely in the urine (from 80 to 92 per cent), principally in the form of inactive metabolic products, 5 to 10 per cent being excreted unchanged. The levels of active material in the urine are appreciably higher than in the blood, but the rise and fall follow the same general pattern. Renal plasma clearance studies indicate that chloromycetin is excreted by glo-

merular filtration, while the conjugate metabolic products are excreted mainly by tubular secretion. The conjugate is probably the monoglucuronide. It is converted back to active chloromycetin and free glucuronic acid by glucuronidase. Incubation with rat liver slices in vitro results in inactivation of the drug, with the formation of nitro compounds and small amounts of arylamines. This phenomenon suggests that the liver is the probable site of conjugation. The rapidity of inactivation and excretion is probably responsible for lack of accumulation in the blood, even with prolonged medication.

Chloromycetin is conveniently administered orally. An initial dose of 60 milligrams per kilogram of body weight is recommended. This large dose may be divided into 2 or 3 parts and given at 1 hour intervals. Maintenance medication, in doses of from 0.25 to 0.5 gram every 3 to 6 hours, may be given during the febrile period and for 5 to 10 days thereafter. Infants or children are given doses of 50 to 100 milligrams in No. 5 capsules.

The drug may be given intramuscularly in 20 per cent polyethylene glycol solution or in peanut oil suspension, but these techniques are not recommended because local tissue reactions are severe (4). Chloromycetin for intravenous use is presently in the experimental stage. No preparation is available at this time for the administration of chloromycetin intrathecally, intrapleurally, or by nebulization.

TERRAMYCIN (36)

Terramycin, an organic base isolated from the Streptomyces rimosus in 1950 by the Pfizer laboratories, has received a wide and extensive preliminary clinical trial (23). It is an amphoteric substance, yellow in color, and is usually produced as the hydrochloride and sodium salts. Although the hydrochloride is soluble in water, free terramycin, which is rather insoluble, is soon released. Dilute solutions of the hydrochloride are stable in acid media. Dried preparations of the sodium salt, the hydrochloride, and the free base are stable for many months. The molecular weight of terramycin is about 460. The antibiotic maintains activity in the presence of cysteine, p-aminobenzoic acid, semicarbazide, sodium chloride, glucose, and glutamate.

Terramycin hydrochloride is presently available for oral use in 250 milligram capsules or in a flavored syrup for children, and for intravenous use in a mixture of the hydrochloride and sodium salts in vials containing 250 or 500 milligrams. Several other preparations containing this drug are under investigation.

On in vitro testing, strains of Haemophilus pertussis were among the most sensitive, and the Neisseria gonorrhoeae and Corynebacterium diphtheriae were highly susceptible. Gram-positive cocci were more susceptible than gram-negative bacilli. Among the former group alpha hemolytic streptococci and pneumococci, and among the latter salmonellae and shigellae were the most sensitive. Strains of the Staphylococcus aureus vary greatly in sensitivity. Considerable parallelism exists between terramycin and aureomycin sensitivities. Organisms resistant to terramycin, aureomycin, or chloramphenicol commonly show an increased resistance to the other two antibiotics but not to streptomycin; strains resistant to streptomycin usually do not exhibit resistance to the other three. The drug shows a high activity against infections experimentally produced by gram-positive cocci, anaerobic bacilli, gram-negative rods, mixed infections (peritonitis), the Rickettsia, and the Endamoeba histolytica.

Following oral administration, terramycin is rapidly absorbed but the serum levels are less than those obtained with chloramphenicol. More terramycin is excreted in both the urine and feces than either aureomycin or chloramphenicol following equal doses of these drugs. Unlike aureomycin, terramycin is fairly stable in serum. No absorption occurs after rectal administration. Terramycin does not diffuse readily into the cerebrospinal circulation. When therapeutic amounts are present in serum, diffusion into the pleural fluid occurs. Terramycin is concentrated in the liver and readily excreted in bile.

Clinical studies indicate that the drug has about the same order of activity as aureomycin against the same list of diseases.

OTHER ACTINOMYCETE-PRODUCED ANTIBIOTICS OF POSSIBLE CLINICAL VALUE

Mycomycin, an antibiotic produced by a mold-like Actinomycete, was reported by Johnson and Burdon in 1947 (34) as being active against some pathogenic bacteria, especially the bacilli of human tuberculosis. This substance is an organic acid of low molecular weight, which is active in vivo, possesses little or no toxicity, and in many respects resembles penicillin. It has not yet been possible to produce a sufficiently stable form of mycomycin to permit its clinical evaluation.

Neomycin was isolated from a Streptomycete in 1949 by Waksman and Lechevalier (74). It is basic, heat stable, and resistant to acid (*p*H 2) hydrolysis. In vitro the drug is highly active against gram-negative organisms as well as strep-

tomycin-sensitive and streptomycin-resistant tubercle bacilli. In lower animals, tuberculosis and gram-negative infections were checked.

The most extensive clinical study to date (71) includes 63 patients with various diseases. The usual dosage was from 1.5 to 2.0 grams per given day, intramuscularly. Proteus infections responded better to neomycin than to any other antibiotic yet studied. However, the toxicity of this drug is the limiting factor in its use at present. Granular casts regularly appeared in the urine during or following treatment but soon disappeared. The blood urea nitrogen increased only in the patients in whom it was elevated prior to treatment. In addition to these renal effects, an ototoxic effect was found in 8 per cent of the cases, which differed from that of streptomycin in that the auditory portion of the eighth nerve was affected before the vestibular. In over half of the patients having symptoms due to involvement of the eighth nerve, total deafness ensued. These symptoms did not occur until 1 to 2 weeks after treatment was stopped; therefore the auditory status of the patient is of no value as an indication to stop the drug. Treatment for as short a time as 4 days may produce deafness. While the possibility exists that some of this toxicity is due to impurities, in view of the basic similarity of the drug to streptomycin, this appears unlikely. It is unfortunate that those infections in which the drug shows most promise are urinary infections and that the nephrotoxic and ototoxic effects are much more prominent in patients with impaired renal function. At present it would appear that:

1. Neomycin may be of value when a severe Proteus infection which does not respond to other drugs is present.

2. Renal function tests should reveal no insufficiency.

3. The dosage should be limited to 1 gram per day.

Neomycin has marked rapid suppressive action in the gastrointestinal tract, from which it is unabsorbed (48).

Viomycin (24, 32, 78), described in 1950, is, like most of the newer antibiotics, produced by a Streptomycete. Its potential importance lies in the finding that in vitro and in vivo in mice and guinea pigs it is highly effective against mycobacteria. In vitro it appears neither synergistic nor antagonistic to streptomycin. The material is a strong organic base which forms neutral salts, the sulfate being the most important. This salt is highly soluble in water and stable at *p*H 5 to 6 for at least a day at room temperature. Like streptomycin, viomycin contains guanidine groups. In addition, it contains a reducing sugar and a peptide linkage. In experimental animals the drug is at least as effective as streptomycin in controlling tuberculosis, although larger doses (quadrupled) are required. It is equally effective against streptomycin-sensitive and streptomycin-resistant strains. The drug is absorbed either orally or parenterally, but as only limited quantities are available to date, the intramuscular route has been utilized. No local reaction is found from the sulfate.

Doses of 50 milligrams per kilogram per day in a number of animal species revealed only vestibular dysfunction in cats after 34 to 45 days. No renal involvement was observed.

In a clinical study of 10 patients with far advanced tuberculosis, from 30 to 75 milligrams of viomycin per kilogram per day were given intramuscularly for up to 6 months. Renal irritation was found in all cases, abnormalities of serum electrolytes in 5 patients, slight elevation of the blood urea nitrogen in 4 patients, impairment of vestibular function and partial deafness in 2 patients, and minor hypersensitivity reactions in 2 patients.

The electrolyte changes included hypopotassemia, hypocalcemia, hypophosphatemia, hypochloremia, and an increase in the carbon dioxide combining power. These changes required discontinuance of the drug in 4 patients and replacement therapy with potassium and calcium salts.

Although clinical improvement of the tuberculosis in these patients was not significant, a trial of viomycin in early cases of tuberculosis is believed to be indicated. The toxic features do not appear severe and are amenable to correction in most instances.

POLYPEPTIDE ANTIBIOTICS

Gramicidin (tyrothricin), the first modern antibiotic to be produced in pure form, was obtained by Dubos (15) from Bacillus brevis cultures by purification of the crude mixture, tyrothricin. It was this work which stimulated general interest in antibiotics as potential chemotherapeutic agents. These antibiotics were shown to be preferentially bactericidal against gram-positive organisms, but they also displayed a hemolytic action which, among other toxic features, prevented their systemic use.

Gramicidin is a cycle peptide containing a number of residuents of varying amino acids, some of d-configuration (16). The mechanism of its action and the significance of the d-amino acids remain obscure. Recent preparations containing dispersing or surface tension agents have enhanced

the chemotherapeutic activity of tyrothricin for topical use. Preparations are available for use as coughdrops (0.25 milligram troches), with an added vasoconstrictor for use in the nose (0.005 per cent solution), and as ointment (0.25 milligram per gram) for use in superficial skin conditions such as impetigo or other pyoderma.

Bacitracin, which is elaborated by a Bacillus subtilis organism tentatively identified as Bacillus licheniformis, was reported in 1945 by Johnson, Anker, and Meleney (33). In 1948, Barry, Gregory, and Craig found that it is a polypeptide (45). It contains predominantly phenylalanine, leucine, isolencine, glutamic acid, lysine, histidine, aspartic acid, and cystine. The material is commercially available as a light tan lyophylized powder that is freely soluble in water, with an activity of about 50 units per microgram. Units are based on the ability of the material to inhibit a strain of hemolytic streptococci. Bacitracin when dry is stable at room temperature, while solutions are stable under refrigeration for more than 2 weeks.

Although duplicating the antibacterial spectrum of penicillin, bacitracin possesses certain additional advantages. Bacteria subjected to its action are not apt to become drug-fast. It is not destroyed by bacteria which produce penicillinase. It is a large polypeptide molecule and is eliminated slowly, so that administration is necessary only every 6 or 8 hours. It has practically no allergenic action. It is readily effective locally against coccal infection. It shows promise in the treatment of ulcerations and granulomas of the colon caused by the Endamoeba histolytica. The chief disadvantage of bacitracin is nephrotoxicity proportionate to the dosage and purity of the batches (53).

Bacitracin is a valuable local agent for coccal infections. It has been found extremely effective in the arrest and control of experimental gas gangrene in guinea pigs, although the renal irritation produced by larger doses of preparations presently available limit its usefulness against this infection in man (55). Systemically administered small doses given with penicillin, exert synergistic action on bacteria only moderately sensitive to either agent alone. Up to 80,000 units daily may be administered, precautions being taken against severe renal damage by repeated blood chemistry determinations and urinalyses (45). Available preparations are similar to those listed under gramicidin.

Polymyxin, a polypeptide of bacillary (Bacillus polymyxa) origin, is of interest because it is highly effective against gram-negative organisms including, with the exception of Proteus, those resistant to streptomycin (38, 65). It has the advantage that organism resistance does not develop. It has, however, a narrow margin of safety, and when it is given in excess of 2.5 milligrams per kilogram per day for more than 5 days, tubular nephrotoxicity may ensue (52).

Polymyxin is the most potent of these drugs currently available against pyocyaneus infection. Topically applied, 1 per cent polymyxin effectively routs gram-negative surface infection if dead tissue is not present in abundance (52). The drug is not absorbed into the circulation following oral administration and its antibacterial action on gram-negative fecal flora is marked.

FACTORS OF INFLUENCE IN ANTIMICROBIAL THERAPY

In the foregoing sections, data have been presented regarding the antimicrobial spectra and the pharmacological properties of antibiotics. From these, it is evident that it is now necessary, and will become so increasingly as the list of antibiotics grows, to have a clear concept of their specificity as therapeutic agents. Before indicating the current place of the individual antibiotics in therapy, factors influencing response to specific treatment will be discussed.

1. *The sensitivity of bacteria to the chemotherapeutic agent.* Specific therapy can be instituted only when precise clinical diagnosis has been established. Isolation of the causative organisms and their sensitivity to chemotherapeutic agents require the services of a bacteriologist. While there are several methods for the determination of culture sensitivity, the Petri plate, medicated disc method is the simplest (Fig. 1). It consists of spacing, over the swab-streaked surface of an agar plate, discs containing measured amounts of each antibiotic tested. Range of sensitivity is determined by the size of the (clear) zone of no growth about the disc; resistance is indicated by the absence of this zone.

In general, an antibiotic is likely to be effective clinically only if the in vitro test shows the organism to be sensitive to a concentration of drug which can be obtained in the blood serum of the patient. Routine multiple culture sensitivity testing demonstrates (1) the variation in sensitivity between different genera as well as between the species and even strains within species, (2) the overlapping antimicrobial action of the different antibiotics, and (3) the emergence during treatment of drug-resistant mutants or of added infection. Culture sensitivity data not only serve as guides to the probable drug of choice, but also furnish clues to the probable dosage required.

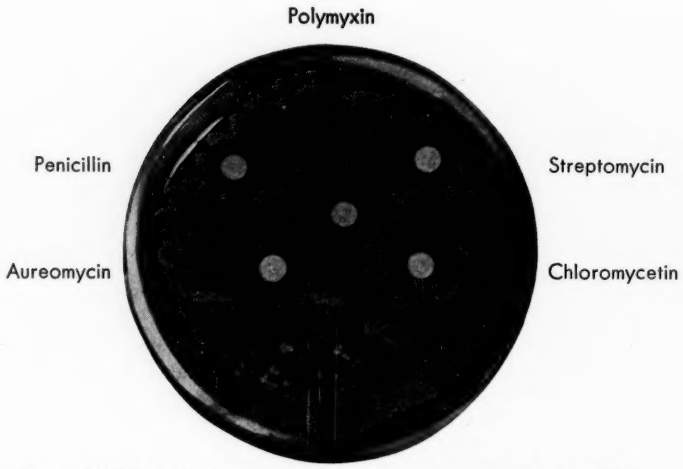

Fig. 1. Multiple antibiotic culture sensitivity testing; medicated disc method.

Prompt discovery of resistance to one antibiotic affords the opportunity for change to an effective alternative agent. Thus, aureomycin, bacitracin, chloromycetin, and streptomycin overlap with penicillin against many gram-positive bacteria, and aureomycin, chloromycetin, and polymyxin overlap with streptomycin against many gram-negative bacteria (Fig. 2).

From a practical point of view, routine sensitivity tests are not absolutely necessary when rapid and precise clinical diagnosis of infectious disease can be made at the bedside, but this is by no means easy. It is worth recalling that the direct smear, often overlooked, can yield invaluable aid in clinical diagnosis. It is suggested that the aid of the bacteriologist be enlisted in the following:

a. Severe infections.
b. Staphylococcal infections, particularly subacute and chronic forms.
c. Nonhemolytic streptococcal infections.
d. Acute gram-negative bacillary and mycobacterial (T.B.) infections.
e. Chronic infections.
f. Infections not responding to treatment as expected.
g. Infections in which the etiologic diagnosis is in doubt.

Antimicrobial therapy should be begun as early as possible, and the therapy should be adjusted or altered when the results of in vitro tests are available.

2. *Drug resistance.* Ehrlich demonstrated that resistance of trypanosomes to drugs can occur by repeated passage through low concentrations in vivo as well as in vitro, and that this resistance, once acquired, is permanent and specific for each class of drug. Organisms resistant to organic arsenicals remain sensitive to azo dyes, and vice versa. He proposed the following solutions to the stumbling block of drug resistance in clinical practice: (1) elimination of all organisms as rapidly as possible, and (2) taking advantage of the absence of cross-resistance by employment, when possible, of drug combinations. The conclusions at which he arrived from his work with the arsenicals are confirmed today with antibiotic and chemotherapeutic drugs.

Resistance to chemotherapeutic drugs can be shown to occur regularly when bacteria are grown in the presence of sublethal concentrations of the drug (14). Development of resistance is independent of the host. It is not the patient who develops the resistance, but the bacteria which, under certain circumstances, become refractory to further chemotherapeutic action.

Resistance of bacteria to drugs is encountered in two distinct forms:

1. Naturally insensitive strains are present in varying degrees in all bacterial populations.

2. Spontaneous mutation occurs during the period of contact with the drug by bacterium. These mutants have lower metabolic activity than the parent strains.

Resistance to penicillin (as to the sulfonamides) proceeds stepwise, with selection at each step to yield populations of higher and higher degrees of resistance. For this reason, when penicillin re-

sistance does develop during the course of infection, it proceeds slowly and ordinarily can be overcome by increasing the dose. Drug-resistant organisms in practice are a clinical problem in a few staphylococcal infections (particularly chronic), nonhemolytic streptococcal endocarditis, and rarely in hemolytic streptococcal and pneumococcal infections.

Drug resistance is of major clinical importance in streptomycin therapy. The predominance of drug-resistant bacteria is not uncommon under conditions in which unhealed lesions persist and drug administration is maintained. In vitro bacteria can even become dependent on streptomycin for growth, but not in vivo. According to Demerec and others, drug-resistant bacterial variants are born periodically by a mutation-like process. In a patient under treatment with streptomycin, the unique property of drug resistance then endows these mutants with a defense mechanism against streptomycin for survival, while streptomycin-susceptible bacteria may be eliminated. If the infection is sufficiently prolonged (as in tuberculosis, in which anatomical factors interfere with healing), the drug-resistant variant eventually may become the predominant member of the population. At this stage further streptomycin therapy becomes useless. It is, therefore, extremely important in subacute and chronic cases to determine culture sensitivity at regular intervals, as a guide to therapy and to reserve streptomycin for infections known to be benefited by its use. As pointed out by Alexander, the rate of resistant mutants is so low for Haemophilus, Escherichia coli, and Shigella organisms that they cannot be expected to play a significant role in the development of resistance to streptomycin. No case of streptomycin-resistant tularemia has yet been reported. Therefore, the drug should still be considered favorably in the treatment of these infections.

Bacterial resistance to aureomycin, chloromycetin, and terramycin may occur in vitro and in vivo. In vivo resistance is usually associated with failure of treatment. It is of considerable interest that organisms becoming resistant to aureomycin also become resistant to chloromycetin and terramycin, and vice versa. The mechanism of this cross resistance is not yet explained (46). Resistance to these drugs is more like that to penicillin than that to streptomycin.

3. *Contact between bacteria and the antimicrobial agent.* Antibiotics administered by mouth or intramuscularly depend on the bloodstream to reach the infection, and are correspondingly ineffective in areas in which the circulation is inadequate. Consequently, antimicrobial therapy can be expected to play a part only when circulatory access to the infected areas is adequate. Accessibility of infection, therefore, will largely determine the form of therapy to be employed. Parenteral therapy is employed in infections involving the blood stream, lung parenchyma, biliary tree, peritoneal cavity, urinary tract, and non-necrotic soft tissue. It is important to remember that antibiotics do not diffuse readily into the brain and bone, and that diffusion into the ocular, cerebrospinal, synovial, pleural, and pericardial fluids is slow and in much lower concentrations than in the blood. Parenteral therapy, then, is supplemented on proper indications: in ocular infections by local or subconjunctival instillation; in empyema, joint space, and walled-off abscess by local therapy; in infections of the tracheobronchial tree by inhalations or aerosols; and in superficial infections of the skin or eyes, by topical application.

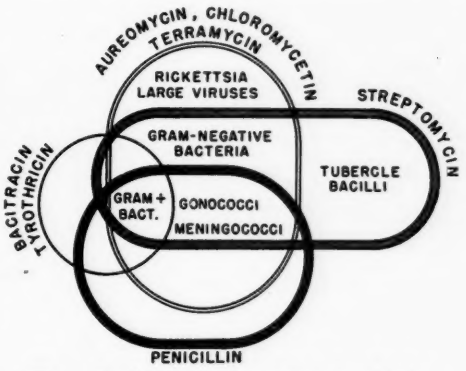

Fig. 2. Overlapping in vitro action of antibiotics.

4. *Adequacy of dose and duration of administration.* Antibiotic dosage varies with the sensitivity of the organism, and the stage, severity, and type of infection. With penicillin, procaine penicillin G preparations, from 300,000 to 600,000 units, given intramuscularly provide much the simplest means of treating early acute infections such as the cellulitides. What they will not do is to produce a high blood level. If the infection is a relatively resistant or severe one, then large doses of penicillin G aqueous should be given. Thus, certain staphylococcal (bacteremia), clostridial (gas gangrene), mixed (acute diffuse peritonitis), and other infections (actinomycosis) may require massive doses of penicillin (1,000,000 units alone, or multiples thereof), or in combination with some other drug for synergistic action. Except in the

instance of subacute bacterial endocarditis, massive doses of penicillin are now preferred to renal excretory blockade with "benemid" for infections requiring high blood levels. Penicillin is given by mouth in a dosage from three to five times the intramuscular dose to achieve the same effect; absorption is irregular, but better when the stomach is empty, and is more constant in infants than in adults. Oral administration of penicillin has a place in the treatment of mild surgical infections in infants and in adults when it is desirable to avoid injections, but we are reluctant to employ it in serious cases because of the uncertainty of its effects.

Streptomycin given by mouth is neither absorbed nor destroyed and is so given only in order to produce an effect in the intestinal tract itself. To obtain a systemic effect, streptomycin is given by intramuscular injection. The dosage (of the dihydro derivative), for short term courses is 1 to 3 grams per day, and for long-continued treatment it is now more commonly 1 gram. The maximal intrathecal dose of streptomycin is 100 milligrams for an adult.

Aureomycin, chloromycetin, and terramycin are given almost exclusively by mouth, beginning with a 2 grams priming dose which is followed by 0.75 to 0.5 gram every 6 or 8 hours. In any condition in which the oral route is barred, special forms of these drugs may be given intravenously. The dosage is from 0.5 to 1 gram dissolved in 250 cubic centimeters of 5 per cent dextrose solution and given twice daily. Antibiotic therapy should be continued in surgical infections until all symptoms and signs of infection have disappeared, or until the temperature and pulse have been repeatedly normal for at least 24 hours. Withdrawal of therapy too soon may be followed by recurrence of the infection.

Combined therapy is often resorted to with the hope that two agents will be more effective than one, either synergistically or at least additively. The reasons for employment of combined therapy (51) are:

1. Moderately resistant organisms. There is suggestive clinical evidence that penicillin and streptomycin are more potent when used in combination for the treatment of Streptococcus faecalis subacute bacterial endocarditis than penicillin is when used alone.

2. Better diffusion. Aureomycin given by mouth and dihydrostreptomycin given intramuscularly are reported to be more effective in the treatment of brucellosis than aureomycin alone; penicillin and sulfonamide combined are said to be needed for actinomycosis.

3. Mixed infections, e.g., peritonitis, empyema, lung abscess, some urinary tract infections, and some infected wounds.

4. Prevention of appearance of drug-resistant organisms: e.g., streptomycin and para-aminosalicylic acid in tuberculosis.

The possibility that penicillin with aureomycin, chloromycetin, or terramycin in combination may cause certain mutually susceptible bacteria actually to grow at a greater rate or show slower killing is now undergoing investigation, and such combinations probably should not be employed without laboratory proof that the combination is not antagonistic. It is essential when combined therapy is employed that maximal therapeutic doses of the drugs be initiated and maintained until the optimal therapeutic response has been effected. Economy by reduction of the dosage is not indicated and may give rise to drug resistance.

5. *The possible alteration of microbial flora during antibiotic therapy.* It has been observed frequently that during the course of treatment with an antibiotic, a change in microbial flora may occur (7, 77). Under these circumstances, while the pathogens sensitive to the antibiotic in use disappear or become less numerous, other organisms may appear in large numbers and cause a new infection. Changes of this kind are apt to occur particularly in the throat, tracheobronchial tree, lungs, gastrointestinal tract, and body surface or in wounds connected with the body surface, such as burns, fistulas and large open wounds. Frequent clinical observation of the patient, together with repeated careful bacteriologic examinations before and during treatment in order to detect the presence of added infections, is therefore important in any antibiotic regimen.

6. *Untoward reactions.* Toxicity attributed to antibiotic therapy, broadly speaking, is of two kinds. One kind bears a definite relation to dosage. The other falls into the category of sensitivity phenomena and is not strictly related, either in incidence or severity, to the amount of drug administered. Either type may occur after brief or prolonged use.

A unique property of penicillin is that it is nearly completely innocuous in character in the face of fantastically high doses. On the other hand, intrathecal injection may—like direct cortical application of either penicillin or streptomycin—lead to convulsive phenomena of an unknown mechanism. The incidence of clinical allergic reactions to injections of penicillin is between 1 and 2 per cent (37). Reactions occur

most frequently in patients who have had several courses of penicillin, and antihistamine therapy may or may not control them. Sensitization reactions may arise following the application of penicillin to the skin or conjunctivae. Some patients may react at the site of previous trichophyton infections following the injection of penicillin, which suggests that there is a common antigen in these two materials. The incidence of reactions to procaine penicillin, particularly the aqueous form, is low. Penicillin "O," recently introduced, is said to be useful and nonallergenic in the penicillin-sensitive patient (59, 69).

Penicillin, like streptomycin, may produce sensitization phenomena. These include eosinophilia, skin eruptions, and arthralgia. Rashes may disappear on continued treatment or get worse, in which case the drug must be discontinued. Dihydrostreptomycin may be useful in the occasional patient with hypersensitivity to streptomycin. Dermatitis venenata, particularly on the hand and forearms, may occur among individuals who handle streptomycin constantly. The most disturbing and most serious reactions following streptomycin are reactions of the eighth nerve, vertigo, tinnitus, and deafness. With the improvement in purity of streptomycin and with the development of dihydrostreptomycin the incidence of these reactions has decreased. Patients who now receive streptomycin for less than 2 weeks rarely develop disturbances of the eighth nerve. Vestibular dysfunction in patients with tuberculosis who receive 1 gm. per day for 42 days is 10 per cent or more; the incidence is said to be lower with dihydrostreptomycin on this dosage schedule.

The most troublesome reactions reported for aureomycin, chloromycetin, and terramycin are nausea and vomiting, sometimes associated with epigastric distress and with a burning feeling in the rectum. The use of aluminum hydroxide to alleviate these symptoms is contraindicated because it interferes with absorption of the antibiotic into the circulation (70). The use of plain or chocolate milk instead of water to swallow the capsules will usually permit ingestion of these drugs without accompanying gastrointestinal distress. One peculiar effect of the administration of these drugs, which results from the bacteriostatic action on the bacteria of the bowel, is the production of soft, bulky, frequent, and almost odorless stools. Mucous membrane changes, colitis and proctitis, which may also complicate therapy, are attributed to the destruction of intestinal bacteria and local alterations of the bacterial flora, often with overgrowth of Monilia. As a rule, patients who cannot tolerate these drugs by mouth experience no unpleasant effects when they are given intravenously. Occasional patients exhibit mild transient euphoria after large doses of chloromycetin, and some experience difficulty with the muscles of accommodation. Leucopenia, which is very infrequent, shows spontaneous reversal even in the face of continued administration of the drug. As with all known antibiotics, skin rashes appear in the occasional patient during aureomycin, chloromycetin, and terramycin therapy.

7. *Resistance of the host.* As has been pointed out before, antibiotics are primarily bacteriostatic in action. Recovery from infection in man, therefore, rarely can be attributed directly to the action of the drug. There is ample clinical and experimental proof that the final destruction of significant proportion of invading organisms depends in most instances on the combined action of the antimicrobial agent and the natural defenses of the host (42, 76). In the untreated patient, the progress of the disease depends upon the ability of the host to localize infection and neutralize the invading bacteria and their damaging effect upon the tissues. The result, therefore, is measured in terms of tissue sacrifice, impairment of function, and time-consuming loss from work or activity. In other words, a patient may recover completely without sequelae except for possible scar tissue formation, or he may go into a state of symbiosis with the infecting organisms (chronic infection) and have recurring acute exacerbations of the original infection or ultimate complete resolution. The main object of specific therapy, therefore, is to cure quickly and completely, with a minimum of tissue sacrifice, so that there will be little likelihood of recurrence. Effective antimicrobial therapy reverses the process of infection and inaugurates healing, but always in proportion to the degree of tissue damage already present. If therapy is delayed, recovery must begin under the added handicap of tissue damage (42).

From the foregoing it is obviously illogical to presume that antibiotic control of infection is all that is required. In severe acute infection reduction in blood volume is not unexpected; in chronic infection nitrogen imbalance, shrunken blood volume, and vitamin depletion are usual concomitants (40). Nutritional deficiency has been shown not only to impair antibody formation but also to lessen the phagocytic powers of leucocytes. The well known impaired resistance of diabetic patients to infection is another instance of the influence of disturbed metabolism. The impor-

tance of restoring and maintaining patients in positive physiologic balance is obvious. Chemotherapy, therefore, is no indication to dispense with supportive therapy, which is just as urgently needed when the former is employed as when it is not.

Due consideration must be given to the effects of ACTH (anterior pituitary adrenocorticotrophic hormone) and cortisone (11 dehydro-17 hydroxy corticosterone-21-acetate) on the host. Antibiotics act upon the micro-organisms by preventing growth and perhaps making them more susceptible to antibody and phagocytic action. ACTH and cortisone, in contrast, act only on the host and, by an undetermined mechanism, prevent the normal antigen-antibody reaction. Since many symptoms of infection appear to be due to antigen-antibody combination, it is to be expected that the prevention of such a combination will produce symptomatic relief; this has been clearly demonstrated to occur with these drugs. On the other hand, the survival mechanisms of the host are adversely affected by the inhibition of antibody action against these micro-organisms. Experimental findings are appearing to support this concept. Initial trials with ACTH or cortisone showed dramatic symptomatic relief in many infectious diseases. However, it was found in treating typhoid fever with cortisone that the incidence of positive stools was unchanged with treatment. When cortisone was used with chloromycetin, the patients responded much more rapidly than when they were treated with the antibiotic alone, but the relapse rate was higher (62, 80). In tuberculosis in the rabbit, it was found that while cortisone markedly decreased the reaction surrounding the tubercles, many more tubercles were present with small inocula of tubercle bacilli, and these contained more bacilli than the controls (39). In an experiment with mice, spontaneous Corynebacterium infection appeared in animals treated with cortisone but not in the controls (6). In view of these experimental and theoretical considerations, it would appear best, at present, to restrict the use of these hormones to those diseases which involve hypersensitivity alone without micro-organisms.

8. *Nature of the lesion.* Surgical infection may be present as wound contamination, as in traumatic wounds and burns; invasive infection, as in spreading cellulitis, and wound suppuration, as in postoperative wound abscess. Included among the bacteria contaminating open wounds or causing invasive infection are the hemolytic streptococcus, hemolytic staphylococcus aureus, the coliform bacilli, and the toxigenic clostridia. Pure coliform or mixed infection may be present in urine, bile, and cerebrospinal fluid, as well as in the peritoneal or thoracic cavity and in open wounds. To be effective, antibiotic therapy must be combined with free flow in the fluids mentioned and with free drainage in cavities and wounds. Most bacteria causing acute infections are extracellular parasites. Once they are ingested by phagocytic cells they are promptly destroyed. Invasive or spreading infection will resolve with little or no necrosis if the appropriate antibiotic is given early. The period of optimal response is seldom in excess of 3 days, although longer periods of treatment are often necessary. Incision and drainage are reserved for small fluctuant areas and the occasional case of massive inflammation requiring decompression (fasciotomy for clostridial myositis). Large abscesses and suppurative lesions are particularly resistant to antimicrobial therapy. The failure of leucocytes (79) to destroy all the bacteria in large accumulations of pus is caused by at least two factors: (1) the absence of normal tissue structures in abscessed areas deprives the leucocytes of the surface upon which they operate most effectively, and (2) leucocytes deprived of oxygen quickly become nonmotile and lose their phagocytic properties. Since the only sources of oxygen in a purulent focus are the intact capillaries at the periphery of the lesion, it is not surprising that all the bacteria in pus are not destroyed when an antibiotic is administered. The indications for surgical drainage of pus, therefore, have not changed. Furthermore, frequent critical examination of the patient receiving antibiotics is more important than ever before. The improvement and freedom from pain which result from specific therapy may mask the true situation, and failure to detect large abscesses (in the body cavities) and to provide drainage may jeopardize not only the patient's health, but also his life (13). It is possible occasionally to sterilize small collections of pus by injecting bactericidal quantities of drug into the focus. This objective is the basis for therapy in such conditions as brain abscess, thoracic empyema, pyoarthritis, and cutaneous abscess.

In wound suppuration the bacterial flora may be heterogenous more often than monobacterial. It is of importance to recall that blood clots, serum, and devitalized tissue perpetuate infection, and that bacteria will thrive behind obstructive barriers and scar tissue. Dead and contaminated tissue will undergo decomposition regardless of the amount and number of antibiotics and irrespective of whether they are administered sys-

temically or locally. Incision and drainage, resection of devitalized tissue, removal of foreign bodies, protection against secondary (added) infection, elimination of dead spaces and pockets, rest, and immobilization, still play the major role in the management of wound suppuration by bringing about conditions unfavorable for bacterial proliferation. The function of antibiotics in wound suppuration is to deal with the infection that remains after surgical revision. Added infection (dressing inoculation), necrotic tissue residue, foreign bodies, and, above all, blind reliance on antibiotics as a substitute for established time-honored surgical principles are common causes of failures in antibiotic therapy.

Chronic infection usually is not successfully managed by antibiotic therapy. Successful eradication of such infection requires: (1) adequate provision for the drainage of pus, (2) mechanical removal of slough, and (3) provision of a good blood supply with the apposition of clean tissue to clean tissue. The function of antibiotics in chronic infection is protection against possible invasive infection incident to surgical extirpation of the infected tissues. Enzymatic débridement of slough in burns and wounds is now undergoing intensive study.

INDICATIONS FOR ANTIBIOTIC THERAPY IN INFECTIONS

While a detailed clinical consideration of antibiotic therapy in individual diseases is not a part of this presentation, broad indications may be mentioned briefly. Antibiotics in surgery may be administered parenterally or topically, for prophylactic or therapeutic use.

1. *Prophylactic use.* The prophylactic use of antibiotics against infection is widespread, yet controlled studies proving its value are few, and precise definition is needed. "Routine" use of these drugs in "clean" surgery, in which the incidence of postoperative infection is low, is hardly justified unless there is unimpeachable evidence that further reduction in the incidence of infection will be accomplished. Antibiotics are solely adjuvants to surgical competency; their indiscriminate use will not compensate for careless technique or disregard for surgical principles. We suggest the following as possible indications for antibiotic protection against impending infection; these are subject, of course, to clinical judgment and appraisal of the individual case: (a) the open traumatic wound and burn, (b) surgery of the contaminated or infected wound, (c) surgery in patients with organic heart murmurs, (d) resection of lung for suppurative disease (thoracoplasty), (e) surgery of localized tuberculous lesions, (f) intestinal flora bacteriostasis before resection, (g) transplantation of ureters to bowel, (h) patients with agranulocytosis, (i) surgery in which postoperative respiratory infection is a threat, and (j) surgery in patients with diabetes.

2. *Therapeutic use.*

a. Diseases caused by gram-positive or mixed bacteria. Because it is cheap and has no dosage-related toxicity, penicillin continues to be the drug of choice in the treatment of acute gram-positive coccal, bacillary (anthrax), clostridial, and actinomycotic infections. Early chemotherapy in cellulitis, carbuncles, lymphangitis, erysipelas, Ludwig's angina, acute secondary parotitis (4), hematogenous osteomyelitis, and septicemia may resolve these lesions spontaneously, without incision for decompression, or with minimal incision of fluctuant areas. As a result, the mortality and morbidity and the length of the hospital stay are reduced materially by their use. Many organisms causing these infections are also highly sensitive to other antibiotics, notably aureomycin, chloromycetin, terramycin, bacitracin, and tyrothricin. These agents, therefore, should be resorted to when penicillin has failed or is contraindicated. Aureomycin, chloromycetin, and terramycin are current drugs of choice for nonhemolytic streptococcal infection.

Antibiotics have proved of little value in the management of tetanus, but experimental evidence supports their prophylactic and therapeutic use to control secondary infection and pneumonia. In gas gangrene, massive doses of penicillin, up to 500,000 units given intramuscularly every 2 hours, are employed to prevent spread of the infection after amputation or fasciotomy and muscle resection.

Staphylococcal or mixed infections in sutured wounds require special consideration. These wounds should first be re-opened, their edges spread apart to the size of the cavity, then loosely packed with gauze, and dressed so as to avoid the danger of secondary infection. When the wounds are clinically clean, they may be repaired secondarily. In "human bites" the results are very good if the patient is seen early (in 6 to 8 hours), but if treatment is started late and there is already joint involvement, surgical drainage is required and the morbidity is prolonged. Antibiotics reduce the invasive character of these infections. Infection in penetrating wounds of joints can be treated safely by immobilization and large doses of antibiotics. Aspiration of exudate and instillation of penicillin to supplement parenteral administration are recommended.

Bacitracin and tyrothricin complex, because they do not cause hypersensitivity, are finding increasing favor in the local treatment of external ocular, nasopharyngeal, cutaneous, and wound infections caused by susceptible bacteria. The use of bacitracin intrathecally for (coccal) pyogenic meningitis and parenterally with penicillin for synergistic action on invasive infections is now under study.

Postoperative infection of the respiratory tract may follow massive collapse, aspiration, or trauma. Prompt diagnosis, bronchial aspiration with reaeration of the lung, and chemotherapy will usually correct atelectatic pneumonia in a few days. Aureomycin, terramycin, and chloromycetin apparently are fully and equally effective and probably preferable to penicillin because of their broader spectra. Early pulmonary abscess usually is managed effectively by antibiotic therapy. Surgery is reserved for the patient who does not respond to antimicrobial therapy.

Successful treatment of established peritonitis is dependent upon prompt diagnosis and early operative repair or removal of the primary source of infection. The use of streptomycin, 0.5 gm. given intravenously by drip with penicillin, 1,000,000 units, twice daily, is usually more effective than either of these agents used singly. Terramycin and aureomycin used singly are also effective agents (56).

We consider preoperative intestinal antisepsis of value, particularly in elective surgery of the left colon. Four agents are reliable intestinal antiseptics when used orally *in conjunction with low residue diet and enemas:* (1) aureomycin or terramycin, 2 gm. daily for 3 to 5 days (8, 56); aureomycin or terramycin have the added advantage that simultaneous blood and intestinal levels are achieved, (2) neomycin, 4 to 6 gm. daily for 3 to 5 days (48); (3) streptomycin with glucuronolactone, 2 gm. each daily for 2 to 4 days (55).

b. Diseases caused by gram-negative bacilli. Streptomycin was the first antibiotic to find extensive application in the treatment of numerous diseases caused by gram-negative organisms. Laboratory and other hospital facilities are required because of (1) wide variation in culture sensitivities, (2) rapid development of resistant strains if infection is not brought under control rapidly, and (3) the well known toxic potentialities of this drug. Although indications for its use may be numerous, grounds for the administration of streptomycin are less weighty since aureomycin, chloromycetin, and terramycin have become available. Streptomycin is still useful against the Escherichia coli, Haemophilus, Shigella, Klebsiella, and Pasteurella tularensis infections (50). Infection of the urinary tract is usually caused by coliform organisms, for which the newer antibiotics are often effective. It is reiterated that permanent beneficial effects are dependent upon a free flow of urine. Polymyxin and neomycin are promising agents against pyocyaneus infection, but are otherwise of limited application because of nephrotoxic potentialities. Chloromycetin is the only effective drug in typhoid fever. It is valuable in some Proteus infections. The most effective drug in Salmonella infections, particularly carrier states, is undetermined.

c. Disease caused by acidfast bacteria. Of the available antibiotics, only streptomycin and viomycin have been found to be effective against Mycobacterium tuberculosis in vivo. Other agents, such as mycomycin, show promise but are as yet untested. Streptomycin has been found to be more effective when it is supplemented with para-amino-salicylic acid or thiosemicarbazone. Drug resistance is also slower to appear when this combined form of therapy is used.

d. Spirochetal diseases. Penicillin has a remarkable effect upon diseases caused by spirochetes. Aureomycin also has established itself in syphilotherapy, but the potentialities of chloromycetin and terramycin are yet to be defined.

e. Rickettsial diseases. Aureomycin, chloromycetin, and terramycin appear to be highly and equally effective in combating Rocky Mountain spotted fever, typhus fever, quadrilateral or Queensland fever, and scrub typhus.

f. Virus diseases. Acute infections caused by some of the larger viruses, such as lymphogranuloma venereum, granuloma inguinale, and psittacosis, may be treated successfully with aureomycin and, probably, with chloromycetin and terramycin. In primary atypical pneumonia, considered a virus disease, prompt and satisfactory improvement follows the use of aureomycin, chloromycetin, or terramycin. Aureomycin has been used also in measles, infectious mononucleosis, and herpes zoster, but results are still inconclusive.

g. Protozoal diseases. Aureomycin and terramycin are effective drugs in the treatment of amebic colitis, but not amebic abscess. Bacitracin also shows promise in amebic colitis.

BIBLIOGRAPHY

1. Abraham, E. P., and Chain, E. An enzyme from bacteria able to destroy penicillin. Nature, 1940, 146: 837.
2. Abraham, E. P., Chain, E., *et al.* Further observations on penicillin. Lancet, Lond., 1941, 2: 177.
3. Alexander, Hattie E., and Leidy, Grace. Mechanism of emergence of resistance to streptomycin in

five species of gram-negative bacilli. Pediatrics, 1949, 4: 214.
4. ALTEMEIER, W. A. Chemotherapy in Surgery. In Carter, B. N. (ed.): Monographs on Surgery, Chap. I. New York: Thomas Nelson & Sons, 1950.
5. ALTEMEIER, W. A., and CULBERTSON, W. R. Chloromycetin and aureomycin in surgical infections. J. Am. M. Ass., 1951, 145: 449.
6. ANTOPOL, W. Anatomic changes produced in mice treated with excessive doses of cortisone. Proc. Soc. Exp. Biol., N. Y., 1950, 73: 262.
7. APPELBAUM, E., and LEFF, W. A. Occurrence of superinfections during antibiotic therapy. J. Am. M. Ass., 1948, 138: 119.
8. BAKER, HINTON J., and PULASKI, E. J. Effects of terramycin on fecal flora. Ann. N. York Acad. Sc., 1950, 53: 324.
9. BLISS, E. A., and TODD, H. P. A comparison of eight antibiotic agents in vivo and in vitro. J. Bact., Balt., 1949, 58: 61.
10. CHAIN, E., FLOREY, H. W., *et al.* Penicillin as a chemotherapeutic agent. Lancet, Lond., 1940, 2: 226.
11. Committee on Medical Research, O.S.R.D., Washington, and Medical Research Council, London. Chemistry of penicillin. Science, 1945, 102: 627.
12. CONTROULIS, J., REBSTOCK, M. C., and BROOKS, H. M., Jr. Chloramphenicol (chloromycetin) V. Synthesis. J. Am. Chem. Soc., 1949, 71: 2463.
13. CURRERI, A. R., SCHMIDT, E. R., and MANDENHALL, J. T. Role of antibiotics in masking inflammatory processes. Arch. Surg., 1948, 57: 513.
14. DEMEREC, M. Origin of bacterial resistance to antibiotics. J. Bact., Balt., 1948, 56: 63.
15. DUBOS, R. J. Bactericidal effect of an extract of a soil bacillus on gram-positive cocci. Proc. Soc. Exp. Biol. N.Y., 1939, 40: 311.
16. DUBOS, R. J., and HOTCHKISS, R. D. Origin, nature and properties of gramicidin and tyrocidine. Tr. & Stud. Coll. Physicians, Philadelphia, 1942, 10: 11.
17. DUGGAR, B. M., *et al.* Aureomycin—a new antibiotic. Ann. N. York Acad. Sc., 1948, 51: 175.
18. EAGLE, H. Blood Levels, Renal Clearance and Chemotherapeutic Activity, With Particular Reference to Arsenicals and Penicillin. In MacLeod, C. M.: Evaluation of Chemotherapeutic Agents. Chap. II. New York: Columbia University Press, 1949.
19. EAGLE, H., and MUSSELMAN, A. D. Rate of bactericidal action of penicillin in vitro as function of its concentration and its paradoxically reduced activity at high concentrations against certain organisms. J. Exp. Med., 1948, 88: 99.
20. Editorial Board of Monographs on Chemistry of Penicillin. Chemical study of penicillin. Brief History. Science, 1947, 105: 653.
21. EHRLICH, J., *et al.* Streptomyces venezuelae N. Sp., the source of chloromycetin. J. Bact., Balt. 1948, 56: 467.
22. Idem. Chloromycetin: A new antibiotic from a soil Actinomycete. Science, 1947, 106: 417.
23. FINLAY, A. C., HOBBY, G. L., *et al.* Terramycin, a new antibiotic. Science, 1950, 8: 85.
24. Idem. Viomycin, a new antibiotic active against mycobacteria. Am. Rev. Tuberc., 1951, 63: 1.
25. FLEMING, A. On the antibacterial actions of cultures of a Penicillium, with special reference to their use in the isolation of Bacillus influenzae. Brit. J. Exp. Path., 1929, 10: 226.
26. GALE, E. F., and RODWELL, A. W. Amino-acid metabolism of penicillin-resistant staphylococci. J. Bact., Balt. 1948, 55: 161.
27. GARVEY, F. K., CLINE, A. C. and MEADS, M. Chloramphenicol in bacillary infections of the urinary tract. South. M. J., 1950, 43: 85.
28. GRIFFITHS, E., JONES, P. T., *et al.* The comparative merits of sodium and procaine penicillin given infrequently. Brit. Med. J., 1949, 2: 958.
29. HERRELL, W. E. Observations on the clinical use of aureomycin. Proc. Mayo Clin., 1949, 24: 612.
30. HERRELL, W. E., HEILMAN, F. R., and NICHOLS, D. R. Procaine penicillin G (duracillin). A new salt of penicillin which prolongs the action of penicillin. Proc. Mayo Clin., 1947, 22: 567.
31. HERRELL, W. E., and WELLMAN, W. E. Current use of penicillin and streptomycin. Med. Clin. N. America, 1950, 34: 319.
32. HOBBY, G. L., *et al.* The activity of viomycin against Mycobacterium tuberculosis and other micro-organisms in vitro and in vivo. Am. Rev. Tuberc., 1951, 63: 17.
33. JOHNSON, B. A., ANKER, H., and MELENEY, F. L. Bacitracin: a new antibiotic produced by a member of the Bacillus subtilis group. Science, 1945, 102: 377.
34. JOHNSON, E. A. and BURDON, K. L. Mycomycin—A new antibiotic produced by a moldlike Actinomycete active against the bacilli of human tuberculosis. J. Bact., Balt., 1947, 54: 281.
35. KEEFER, C. S. Dosage forms of penicillin for systemic infection. Am. J. Med., 1949, 7: 216.
36. Idem. (ed.) Terramycin. Ann. N. York Acad. Sc., 1950, 53(2)
37. LEPPER, MARK H., DOWLING, H. F., *et al.* Studies on hypersensitivity to penicillin. I. Incidence of reactions in 1,303 patients. J. Clin. Invest., 1949, 28: 826.
38. LONG, P. H., *et al.* Antibiotics derived from Bacillus polymyxa. Ann. N. York Acad. Sci., 1949, 51: 853.
39. LURIE, M. B., *et al.* Constitutional factors in resistance to infection: the effect of cortisone on the pathogenesis of tuberculosis. Science, 1951, 113: 234.
40. LYONS, C. Penicillin therapy of surgical infection in the U.S. Army. J. Am. M. Ass., 1943, 123: 1007.
41. MARSHALL, E. K., Jr. The dosage schedule of penicillin in bacterial infections. Bull. Johns Hopkins Hosp., 1948, 82: 403.
42. MCDERMOTT, WALSH. The Nature of the Lesion and the Response to Antimicrobial Therapy. In MacLeod, C. M.: Evaluation of Chemotherapeutic agents, Chap. VI. New York: Columbia University Press, 1949.
43. MCLEAN, I. W., SCHWAB, J. L., *et al.* Susceptibility of micro-organisms to chloramphenicol. J. Clin. Invest., 1949, 28: 953.
44. MELENEY, F. L. The intelligent use of antibiotics in the prophylaxis and treatment of surgical infections. N. York Med., 1949, 5:15.
45. MELENEY, F. L., and JOHNSON, B. A. Bacitracin. Am. J. Med., 1949, 7: 794.
46. PANSY, F. E., *et al.* The relationship between aureomycin, chloromycetin, and terramycin. Proc. Soc. Exp. Biol., N.Y., 1951, 75: 618.
47. PECK, R. L., BRINK, N. G., *et al.* Streptomyces antibiotics, crystalline streptomycin trihydrochloride-calcium chloride double salt. J. Am. Chem. Soc. 1945, 67: 1866.
48. POTH, EDGAR, J., FROMM, STANLEY M., *et al.* Neomycin, a new intestinal antiseptic. Texas Rep. Biol. M., 1950, 8: 353.
49. PULASKI, E. J. The place of antibiotics in the field of surgery. Ann. N. York Acad. Sc. 1950, 53: 347.

50. Idem. Use of Streptomycin in Surgical Infections. In Advances in Surgery, Vol. II. New York: Interscience Publishers, 1949.
51. PULASKI, E. J., and BAKER, H. J. Combined therapy of infectious disease. South. M. J., 1949, 42: 765.
52. PULASKI, E. J., BAKER, H. J., *et al.* Laboratory and clinical studies of polymyxin B and E. J. Clin. Invest., 1949, 28: 1028.
53. PULASKI, E. J., and CONNELL, J. F., JR. Bacitracin in surgical wound infections. Bull. U. S. Army M. Dep., 1949, 9: 141.
54. Idem. Procaine penicillin G for aqueous injection. A study of blood and urine levels. N. England J. M., 1949, 241: 514.
55. PULASKI, E. J., CONNELL, J. F., JR., and SEELEY, S. F. Sterilization of the intestinal tract by antibiotics and supplemental agents. Ann. Surg., 1950, 132: 225.
56. PULASKI, E. J., SHAEFFER, JOSEPH R., *et al.* Studies in the Use of Terramycin in Experimental and Clinical Peritonitis. Forum on Fundamental Surgical Problems. Pp. 119-126. Philadelphia: W. B. Saunders, 1951.
57. Report to the Council on Pharmacy and Chemistry, Am. M. Ass. Current status of the chemotherapy of tuberculosis in man. J. Am. M. Ass., 1950, 143: 896.
58. ROSE, H. M., and KNEELAND, Y. Aureomycin in the treatment of infectious diseases. Am. J. Med., 1949, 7: 532.
59. SAMITZ, M. M., HORVATH, P., and BELLETT, S. A hemorrhagic bullous eruption due to penicillin G. Ann. Allergy, 1950, 8: 337.
60. SCHATZ, A., BUGIE, E., and WAKSMAN, S. A. Streptomycin, a substance exhibiting antibiotic activity against gram-positive and gram-negative bacteria. Proc. Soc. Exp. Biol., N. Y., 1944, 55: 66.
61. SMADEL, J. E. Chloramphenicol (chloromycetin) in the treatment of infectious diseases. Am. J. Med., 1949, 7: 671.
62. SMADEL, J. E., *et al.* Treatment of typhoid fever. I. Combined therapy with cortisone and chloramphenicol. Ann. Int. M., 1951, 34: 1.
63. SMADEL, J. E., and JACKSON, E. B. Chloromycetin, an antibiotic with chemotherapeutic activity in experimental rickettsial and viral infections. Science, 1947, 196: 418.
64. SMITH, GRANT N., and WORRELL, C. S. Studies on the action of chloramphenicol on enzymatic systems; effect of chloramphenicol on the activity of proteolytic enzymes. Arch. Biochem., N. Y., 1949, 23: 341.
65. STANSLEY, P. G. The polymyxins; a review and assessment. Am. J. Med., 1949, 7: 807.
66. STEWART, H. C., and MAY, J. R. Absorption of penicillin by mouth. Lancet, Lond., 1947, 2: 857.
67. TUCKER, H. A., and EAGLE, H. The serum concentrations of penicillin G in man following intramuscular injections in aqueous solution and in peanut oil-beeswax suspension. Am. J. Med., 1948, 4: 343.
68. UNGAR, J. Penicillin in tissue exudate after injection. Lancet, Lond., 1950, 1: 56,
69. VOLINI, I. F., *et al.* Use of penicillin "O" in patients hypersensitive to penicillin G. J. Am. M. Ass., 1950, 143: 794.
70. WAISBREN, B. A., and HUECKEL, J. S. Reduced absorption of aureomycin caused by aluminum hydroxide gel. Proc. Soc. Exp. Biol., N. Y., 1950, 73: 73.
71. WAISBREN, B. A., and SPINK, WESLEY W. Neomycin: clinical investigations. Bull. U. Min. Hosp. & Minn. M. Found., 1950, 530: 551.
72. WAKSMAN, S. A. Microbial Antagonisms and Antibiotic Substances. New York: The Commonwealth Fund, 1947.
73. Idem. (ed.) Streptomycin, Its Nature and Practical Application. Baltimore: The Williams & Wilkins Company, 1949.
74. WAKSMAN, S. A., LECHEVALIER, H. A., and HARRIS, D. A. Neomycin: production and antibiotic properties. J. Clin. Invest., 1949, 28: 934.
75. WAKSMAN, S. A., and WOODRUFF, H. B. Streptothricin, a new selective bacteriostatic and bactericidal agent, particularly active against gram-negative bacteria. Proc. Soc. Exp. Biol., N. Y., 1942, 49: 207.
76. Idem. Bacteriostatic and bactericidal substances produced by a soil actinomycete. Proc. Soc. Exp. Biol., N. Y., 1940, 45: 609.
77. WEINSTEIN, L. Spontaneous occurrence of new bacterial infections during antibiotic therapy. Am. J. Med. Sc. 1947, 214: 56.
78. WERNER, CHARLES A., *et al.* Studies on the toxicity of viomycin in humans. Am. Rev. Tuberc., 1951, 63: 49.
79. WOOD, W. B. Defense Mechanisms of the Host In Relation to Chemotherapy of Acute Bacterial Infections. In MacLeod, C. M.: Evaluation of Chemotherapeutic Agents. Chap. 5. New York: Columbia University Press, 1949.
80. WOODWARD, T. E., *et al.* Treatment of typhoid fever. II. Control of clinical manifestations with cortisone. Ann. Int. M., 1951, 34: 10.

ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Familial Fibrous Swelling of the Jaws. JOHN CAFFEY and JOHN L. WILLIAMS. *Radiology*, 1951, 56: 1.

The authors present 5 cases of familial fibrous swelling of the jaws, occurring in members of two families. The disorder is characterized by massive swelling of the cheeks and jaws beginning during the first 3 years of life. Dentition is defective. There are no associated symptoms or systemic manifestations unless the lower jaw becomes so large that it prevents closure of the mouth and interferes with respiration and speech. Roentgenograms show extensive multilocular rarefaction and marked expansion of the mandible. The maxilla is also greatly expanded but the rarefaction is diffuse and even, rather than multilocular. No other bones are affected.

Beginning near puberty, there is an improvement in facial appearance, with a progressive decrease in the size of the jaws; by middle age the roentgen and facial abnormalities are minimal or absent.

Tissue specimens from the jaws show microscopic changes similar to those of fibrous dysplasia, but the clinical and roentgen features of these two diseases differ so markedly that they are considered separate entities. BENJAMIN GOLDMAN, M.D.

Plastic Surgery for Mandibular Retrusion. MILTON THOMAS EDGERTON, JR. *Plastic & Reconstr. Surg.*, 1950, 6: 450.

The authors describe a method of lengthening the soft tissue of the lower jaw by elastic traction and the use of bone grafts for severe mandibular retrusion not suitable for other types of treatment.

The method consists in the vertical division of the body of the mandible through an intraoral incision in the first stage. This is followed by traction on the symphysis with firm elastic traction fixed to a head cap for 3 weeks. Iliac bone is then fixed by stainless steel wire to fill the defect created by the traction. By this means almost double the correction secured when the nerve is preserved can be obtained.

Continuous elastic traction has also been found helpful in the treatment of severe micrognathia in infants. This seems to increase the forward growth of the symphysis. THOMAS C. DOUGLASS, M.D.

Recessive Ramisection of Jaw, Lip and Nose Correction; Corrective Dental Prosthesis in Cleft Lip and Palate Deformity. JAMES BARRETT BROWN, MINOT P. FRYER, and J. B. TEMPLETON. *Plastic & Reconstr. Surg.*, 1950, 6: 441.

The authors describe a technique for recession of the mandible in cases of cleft lip and palate in which patients are too old, or otherwise not suited to orthodontic expansion of the upper arch.

Local anesthesia is preferred with block of the second and third divisions of the fifth nerve.

The ramus is divided between the sigmoid notch and the foramen. A Gigli saw is passed through a 1 cm. skin incision permitting an opening to be made deep to the ramus by means of a modified aneurysm needle, and the ramus is divided without injury to the vessels or nerve. The skin wounds are closed. Then the other side is divided in similar fashion.

The predetermined new position of the jaw is located and fixed by interdental means and rubber bands if necessary. A pressure dressing is applied for 6 days.

The technique of this operative procedure in a case of cleft lip and palate is well illustrated, and described in detail with the various dental considerations. THOMAS C. DOUGLASS, M.D.

EYE

Clinical Trial with Chloramphenicol in Ocular Infections. IRVING H. LEOPOLD. *Arch. Ophth.*, Chic., 1951, 45: 44.

The author presents the results of his clinical experience with chloramphenicol (chloromycetin) in ocular infections.

He points out that four criteria are of major importance in evaluating antibiotics in ophthalmology: (1) ease of penetration into ocular tissues when the drug is locally or systemically administered; (2) toxicity for ocular tissues; (3) effectiveness against standard experimental ocular infections; and (4) effectiveness against clinical ocular infections.

Most ocular infections of bacterial origin can be controlled by available antibiotics, and several conditions of viral origin can also be treated successfully. The choice of antibiotic is guided by culture and sensitivity studies. It should be changed if no improvement occurs in 48 to 72 hours.

Chloramphenicol solution, in a concentration of 2.5 mgm. per cubic centimeter of water, is effective local therapy for conjunctivitis and dacryocystitis. Chloramphenicol is of assistance, systemically and locally, in various forms of keratitis.

The drug was tried in 10 cases of uveitis but its value in this condition was not significant. When administered systemically, intraocular infection was controlled in 3 cases.

Fifteen patients with herpes zoster ophthalmicus responded to chloramphenicol systemically.

JOSHUA ZUCKERMAN, M.D.

Case Notes: A Rodent Cyst. P. O. ELLISON and E. M. G. GALTON. *Brit. J. Ophth.*, 1951, 35: 53.

A case of rodent cyst of the left eyelid in a man 70 years of age is presented.

The cyst, which had been noticed 7 years previously, had reached the size of a large grape. It was situated between the skin and the tarsal plate and extended to the eyelid margin. It transilluminated well. Every few weeks a watery discharge was present.

The cyst was considered to be a cystadenoma of a sweat gland but histologic examination revealed that it was a carcinoma.

It is concluded that the whole picture is an example of a "rodent ulcer" arising in the wall of a keratinous cyst. JOSHUA ZUCKERMAN, M.D.

Neutron Cataracts. ARLINGTON C. KRAUSE and JAMES O. BOND. *Am. J. Ophth.*, 1951, 34: 25.

Cataracts resulting from infrared light, roentgen rays or radium, and electricity produce characteristic lesions in the lens represented by small punctate opacities along the optical axis in the subcapsular regions of the anterior and posterior cortex.

Similar opacities may result from exposure to neutron beams from the cyclotron or nuclear fission explosions.

The clinical and experimental studies of roentgen-ray and radium cataracts are reviewed, recent reports of investigations in the field of neutron cataracts are presented, and the possible pathogenesis of these radiation damages in the lens are discussed.

The clinical and experimental investigations of roentgen and neutron radiation cataracts reveal that (1) both forms of radiant energy damage the anterior epithelial cells of the lens cortex, resulting in the production of abnormal fibers leading to opacities in the subcapsular regions of the cortices; (2) neutrons are more damaging per unit of absorbed energy than roentgen rays so that the latent period is shorter; and (3) oxidation of sulfhydryl groups on the enzymes of normal lens metabolism is a possible mechanism for the biologic effect on the lens structure.

It would be interesting to know the exact data of exposures of neutrons required to produce cataracts, the specific effect of radiation on normal lens metabolism, and the methods of prevention before and after exposure. JOSHUA ZUCKERMAN, M.D.

Retrolental Fibroplasia. ALGERNON B. REESE and FREDERICK C. BLODI. *Am. J. Ophth.*, 1951, 34: 1.

The authors discuss retrolental fibroplasia. They point out that this condition is often confused with other conditions, especially persistent hyperplastic vitreous (tunica vasculosa lentis). Although the incidence of the latter condition is low, material for study is abundant because these eyes are usually enucleated when mistaken for retinoblastoma. Persistent hyperplastic vitreous is unilateral and the involved eye is often slightly smaller then the fellow eye; the opaque tissue behind the lens is densest in the central part and fades in the periphery where long ciliary processes can invariably be seen; posterior cortical cataract usually develops and gradually produces a complete opacity of the lens; secondary glaucoma may ensue, and a persistent hyaloid artery can sometimes be seen.

Retrolental fibroplasia is a clear-cut entity which is characteristically bilateral. It affects primarily premature infants of low birth weights. Two per cent of cases occur in full-term infants. An acute or active phase which subsides at about 3 months of age, and a late or cicatricial stage have been recognized.

The acute phase of the disease, consisting of dilatation of retinal vessels, hemorrhages, neovascularizations, and transudation subsides between the third and fourth months of life and is followed by a stage of organization and contracture (cicatricial stage). It is generally first diagnosed in the late, cicatricial stage when the retina is completely detached and drawn up into contracting fibrous tissue back of the lens.

Retrolental fibroplasia may represent the eye manifestation of a generalized congenital angioplastic process.

The acute stage of retrolental fibroplasia has been benefited by administration of adrenocorticotropic hormone therapy. Between 20 and 25 mgm. of the drug are given each day for 14 days. A second course of treatment was given in 21 cases in which the disease became reactivated after cessation of treatment.

In 14 patients receiving adrenocorticotropic hormone treatment, the retrolental process regressed or was arrested, and in none of the patients treated during the early stages did a partial or complete retrolental membrane develop.

Some late cases may be helped by surgical removal of tissue in the pupillary area to permit the use of any partially attached area of the retina.

JOSHUA ZUCKERMAN, M.D.

Unusual Retinal Detachment, Possibly Sex-Linked ARNOLD SORSBY, M. KLEIN, J. HURNDALL GANN, and G. SIGGINS. *Brit. J. Ophth.*, 1951, 35: 1.

The authors discuss an unusual type of retinal detachment, possibly sex-linked. They describe a family in which there were 8 affected men throughout three generations. The 4 youngest men had cystic detachment of the retina, and 2 (or possibly 3) of the older members had extensive degenerative changes in the fundus, presumed to be the end stages of the condition.

The numerous variations in appearance suggest that cystic detachment is a slowly progressive affection, possibly of congenital origin. Only one eye may be affected and it occasionally takes the form of an abortive falciform detachment or of a mere linear scar. Extensive retinal atrophy generally ensues.

They believe that the affection is sex-linked. They are also of the opinion that congenital total detachment of the retina, congenital falciform detachment of the retina, cystic detachment as seen in boys and

young men, and vascular vitreous veils are different aspects of one and the same entity.

JOSHUA ZUCKERMAN, M.D.

Retinal Detachment and Aphakia. CHARLES L. SCHEPENS. *Arch. Ophth.*, Chic., 1951, 45: 1.

The author discusses retinal detachment and aphakia, and the procedures used for replacement.

Retinal detachment occurs in only 1 to 2 per cent of all cases of cataract extraction. Twenty-three per cent (88 cases) of the total number of detachments treated in the Retina Service of the Massachusetts Eye and Ear Infirmary occurred in aphakic patients. The condition is probably caused by an inflammation or a degeneration in the region of the ora serrata, which is asymptomatic for a long time but eventually causes one or several of the following conditions: mild uveitis without visible foci either in the anterior segment or in the choroid posterior to the equator; posterior cortical opacities in the lens; retinal detachment and deep chamber glaucoma. Changes near the ora serrata without equatorial lesions occurred in 66 per cent of the patients with aphakia. Progressive posterior cortical or posterior subcapsular opacities of the lens are suggestive signs which may indicate that a detachment is to be feared. Vitreous opacities are also suspicious, as is a fine, dustlike vitreous haze, or the sudden appearance, or a sudden increase, of peripheral and fairly coarse vitreous floaters, which may or may not be due to bleeding.

The indirect stereoscopic ophthalmoscope with a scleral depressor is believed to be the most useful instrument for examination of the extreme periphery of the retina. Examination should be performed both in a sitting and in a lying position.

Vitreous retraction was present in 45 per cent of the author's cases. Massive vitreous retraction made the surgical prognosis hopeless and was more than three times as frequent in aphakic eyes as in phakic eyes.

Massive vitreous retraction is characterized by two principal ophthalmoscopic features: (1) all the retinal folds are fixed and when the eye moves they remain immobile, and (2) the fixed retinal folds radiate from the posterior pole of the globe toward the equator. Near the equator, and parallel to it, is a circular fixed fold which makes a sharp ridge in the fundus.

In most of the cases of detachment in phakic patients changes appeared at the equator, but in 65 per cent of detachments with aphakia, lesions occurred in the region of the ora serrata only. Retinal breaks were usually multiple and the majority of them (more than 80 per cent) could not be seen with the usual methods of direct ophthalmoscopy.

In 40 per cent of the cases the first symptoms of detachment occurred within 12 months after the cataract extraction; in 21.5 per cent detachment began before the cataract was extracted. Results were poorer after extracapsular extraction (and after discission of the lens in young patients) than after intracapsular cataract extraction. Loss of vitreous was not a cause of detachment, but made the prognosis poor. Uveitis was present in 23 per cent of cases, but the prognosis was good.

Among 69 cases, retinopexy was successful in 56.5 per cent; of 55 eyes operated on by this method, reattachment was observed in 62 per cent.

JOSHUA ZUCKERMAN, M.D.

EAR

Chronic Exudative Otitis Externa. J. P. STEWART. *J. Lar. Otol.*, Lond., 1951, 65: 24.

This investigation is limited to cases of chronic exudative otitis externa and does not include mycotic lesions or cases complicated by middle ear disease or other disease of the external canal.

External otitis probably originates by infection introduced by contaminated fingers during the act of scratching. Personal hygiene and cessation of scratching the ears would do much to reduce the incidence of external otitis.

Sebaceous, sweat, and sudoriferous glands are found in the wall of the external ear. The ceruminous glands are coarse, modified sweat glands but larger in size. They should not be confused with the sebaceous glands. Histopathologic changes in external otitis cannot be well discussed due to the paucity of material available. In the cases studied, there was no change in the epidermis. Their dermis showed a nonspecific inflammatory reaction in which polymorphonuclear leucocytes predominated. Most of the ceruminous glands were dilated, full of pus, and were surrounded by polymorphonuclear cells. This reaction explains the loss of wax in this disease.

When the bacteriologic findings of the normal were compared with those of external otitis, striking differences were found. From the normal ear canals, several sterile cultures were obtained, a few cases of Staphylococcus albus or staphylococcus aureus, and only 2 cases of Bacillus coli. A few saprophytic organisms were also occasionally obtained. The majority of the cultures from the abnormal ears showed organisms associated directly or indirectly with the intestinal tract. Several organisms were found together.

There are two distinct stages in the healing of the disease. The first stage is concerned with the drying up of the exudative condition; the second stage carried on from this to the healed stage.

In the first stage local antibiotics, sulfonamides, and ultraviolet light were tried. Some success was found with streptomycin, almost none with penicillin, and considerable success with sulfathiazole or ultraviolet light. The antibiotics quite frequently gave severe reactions or exacerbations of the disease.

The second stage is more easily controlled. A successful mode of treatment is the application of gauze soaked in a soothing mildly antiseptic ointment such as ichthyol and zinc oxide in a lanoline base. After such treatment, a prophylactic paint of 27 per cent gentian violet can be used. JOHN R. LINDSAY, M.D.

NOSE AND SINUSES

Exfoliative Cytology as an Aid in the Diagnosis of Tumors of the Throat, Nose, and Ear. I. FRIEDMANN. *J. Lar. Otol.*, Lond., 1951, 65: 1.

Cytology as an aid in diagnosis in otorhinolaryngology is in its early stages. The purpose of the present work was to (a) study the various types of malignant cells and the confusing elements encountered in smears from the ear, nose, and throat in cases of suspected malignancy; and (b) to collect further information on the diagnostic uses and limitations of exfoliative cytology as applied to otolaryngology.

The collection of secretions is most easily accomplished with curved cotton carriers or small gauze swabs. The material is then smeared on microscopic slides and dropped immediately into a vessel containing the fixative of equal parts of absolute alcohol and ether. The slides are fixed in 20 to 30 minutes but can remain in the fixative for any reasonable time.

In order to interpret the smears, a thorough knowledge of the normal cells encountered is imperative. Squamous epithelial cells and columnar respiratory epithelial cells are most frequently found.

Malignant squamous cell carcinoma can be divided into differentiated or undifferentiated malignant cells. The nucleus of a malignant cell is enlarged usually at the expense of the cytoplasm. It is hyperchromatic, with the chromatin being arranged in clumps or coarse strands. The nuclear borders are irregular in outline and may be wrinkled. The nucleoli are enlarged but cannot always be seen. Multinucleated cells are common.

Exfoliative undifferentiated cells occur in both anaplastic and differentiated carcinomas. They represent most commonly cases of lymphosarcoma or reticulosarcomas of the upper respiratory tract.

Exfoliated differentiated cells of squamous cell can be subdivided into: (1) the fiber cell—a thin elongated cell with a long segmented cigar-shaped nucleus (the cytoplasm is acidophilic); (2) the tadpole cell has a "head" and a tail of cytoplasm (the head often contains several nuclei); (3) the "third type malignant cell" has a distinct cellular outline, abundant cytoplasm, and malignant type nucleus (this is the most common cell found).

Results of the smears were remarkably consistent with the findings of biopsies or at autopsy. False negative (smear negative, biopsy positive) reports will always occur. However, false positive (smear positive; biopsy negative) reports can be reduced to a very small percentage. This depends on the skill of the examiners and also the occasional misinterpretation of distorted degenerative or inflammatory cells with malignant cells.

Cytologic examinations are useful when a biopsy is unobtainable either due to location or owing to refusal of the patient. It is of value in the presence of positive clinical signs when the biopsy shows no malignant cells. In cases of carcinoma *in situ* or those of doubtful etiology, it may yield the diagnosis.

JOHN R. LINDSAY, M.D.

Rhinophyma: Plastic Correction. ROBERTO FARINA. *Plastic & Reconstr. Surg.*, 1950, 6: 461.

Rhinophyma is characterized by a tumorous appearance of the nose; it may or may not be multilobular. This is a benign, slow but progressive, hypertrophy of the skin of the lower one-third of the nose. Rhinophyma is generally the end-stage of acne rosacea. The etiology is unknown but there seems to be a relation between accumulation of fat in the sebaceous glands and a lymphatic and venous stasis (histopathologically, hypertrophy of the sebaceous glands, telangiectasis of the blood vessels, and extensive hyperplasia of the connective tissue are found).

Rhinophyma is painless. It may limit nasal respiration mechanically. The chief complaint of patients affected with this disease is disfigurement.

Two types of surgical treatment have been tried.

1. Simple electrosurgical decortication was the first method tried. The area to be excised is delimited with an electrical scalpel; then, with a loop electrotome, the tumorous masses are decorticated progressively until the nose is near normal in size. The osteofibrocartilaginous layer must not be exposed or necrosis may result. Hemostasis is controlled with pressure and electrocoagulation. Postoperatively, sulfathiazole is sprinkled over the wound until a crust is formed. The crust is shed as epithelization occurs. Any granulation tissue formed is cauterized with silver nitrate. Total epithelization occurs in 1 or 2 months.

2. Excision by divulsion with free skin grafting is the second method. Again the mass is delimited with an electrical scalpel, and the mass is then detached by divulsion from the root of the nose down. A split-thickness skin graft is taken from the thigh. The graft is immobilized with cotton and aluminum plate.

The second method is superior to the first. Divulsion is easier and quicker as there is found a line of cleavage. This decreases bleeding, the danger of exposing cartilage is minimized, and scar retraction is not likely. Postoperative care is reduced, even if part of the graft is lost. JOHN R. LINDSAY, M.D.

Nasopharyngeal Malignant Tumor; An Overlooked Condition. HAROLD L. HICKEY. *Arch. Otolar.*, Chic., 1951, 53: 53.

Nasopharyngeal malignant growths comprise about 3 per cent of malignant tumors of the head and neck. The wide variety of initial symptoms, the inaccessibility to examination and biopsy, and wide metastases overshadowing the primary lesion make diagnosis difficult.

Epipharyngeal tumors have been reported in all age groups, the youngest patient, whose case is recorded in the literature, being 2 years of age. The majority of these tumors are found in the age group between 41 and 60. Males are affected more than females. Orientals have been found to have malignant lesions in the nasopharynx more often than Caucasians.

Pathologic descriptions vary widely and are often confusing. Histopathologists today consider carcinoma to be more common than sarcoma in the nasopharynx. Salinger and Pearlman considered that most nasopharyngeal tumors should be classified as transitional cell carcinoma, a few as lymphoepithelioma, and rarely any as sarcoma. Ewing stated that epidermoid or transitional cell carcinoma, when located in a region associated with lymphoid tissue, is difficult to distinguish from lymphoepithelioma.

Hematogenous or lymphogenous metastases first tend to involve the cervical glands, especially the anterior cervical chain. Later, metastases occur to the liver, lung, and osseous system. Local extension by contiguity occurs to the base of the skull. The extension is most often through the foramen lacerum. Involvement of any of the cranial nerves may occur, the sixth cranial nerve being the one most commonly involved.

The symptoms and signs of a nasopharyngeal malignancy are varied and usually do not refer to the primary lesion except by inference. Sarcomatous lesions are often more easily identified as nasal obstruction and bleeding. Epithelial tumors, on the other hand, may give a sign and symptom complex referable to the cervical glands, nose and pharynx, ear, eye, intracranial region, gasserian ganglion, and the jugular foramen. Unilateral cervical lymphadenopathy or cranial nerve involvement may or may not be late signs.

As an aid to diagnosis, nasopharyngeal examination can not be stressed too greatly. Use of the nasopharyngeal mirror with or without the Yankauer speculum, or use of the electric nasopharyngoscope is of great help.

Biopsy of suspected tissue is imperative for diagnosis. This may be quite difficult if the lesion is small. A valuable aid in diagnosis is the x-ray picture. Changes in the sphenoid and temporal bones are often found.

The treatment which has proved most effective is deep x-ray therapy of the primary lesions and cervical metastases, with or without the use of radon seed implantation.

The 5 year survival rate is no greater than 20 to 25 per cent. The sarcomatous lesions are much more radiosensitive and offer the best life expectancy.

Twenty-four cases are summarized in chart form in the original article. JOHN R. LINDSAY, M.D.

Anatomical and Clinical Evaluation of Head Pain Attributed to the Sphenopalatine Ganglion. ROBERT B. LEWY. *J. Lar. Otol.*, Lond., 1951, 65: 10.

In 1908 and 1915, Sluder noted the position of the sphenopalatine ganglion and its close relationship to the sphenoid sinus and posterior group of ethmoid sinuses. Thus, he argued, when the adjacent sinuses are irritated, the inflammatory reaction may spread and involve the ganglionic elements. The characteristic pain area is from the root of the nose, in and about the eye, extending back along the zygomatic arch to the ear. The greatest pain centers 5 centimeters behind the mastoid process. A slight sore throat may also exist. The simple test of cocainization of the ganglion would complicate it as the source of pain.

Disagreement with this hypothesis has been expressed. The specific anatomy and physiology of the constituent parts of the sphenopalatine ganglion and vidian nerve remain partly unknown. Clinical observation has contributed little definitive information. Larsell indicates that both nerves which make up the vidian are motor in function and the sensory fibres of the maxillary nerve pass through the ganglion. Vidian neuralgia, according to this anatomical interpretation, would not be possible. Cocainization in the region of the sphenopalatine ganglion may affect only the maxillary division of the fifth nerve. The author quotes Larsell and Fenton's opinion, that an anatomic solution to this problem of referred pain has not been reached.

JOHN R. LINDSAY, M.D.

MOUTH

Surgery of Monstrous Tumors of the Oral Cavity (Chirurgie des tumeurs monstres de la cavité buccale). VERNIER. *Sem. hôp.*, Paris, 1951, 27: 470.

Four cases of giant tumors of the oral cavity, observed in Sudan, are reported by the author.

All of the patients presented the syndrome of inanition caused by insufficient nutrition, and marked anemia. In 2 patients the tumors originated in the lower jaw; one had a sublingual angiofibroma and the other a submucous fibroma deriving from the palate. One of the tumors in the lower jaw

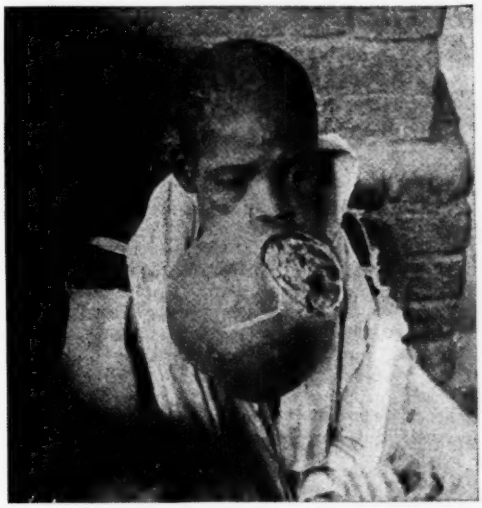

Fig. 1 (Vernier). Tumor of the face extending across the lips, which are very much extended. Note an isolated molar tooth at the center of the ulcerated mucous surface.

was an adamantinoma and the other a mixed angiomyxoglandular formation.

The excision of the enormous tumors required several stages, namely, preliminary tracheotomy, ligation of both external carotid arteries, and, finally, the removal of the formation. On one patient who succumbed to the operation no preliminary tracheotomy or ligation of the carotid artery was done.

As ether is too volatile in warm climates, chloroform was used for anesthesia. Pentothal was not employed because ligation of the carotid artery necessitated a close contact with the carotid sinus.

JOSEPH K. NARAT, M.D.

PHARYNX

Treatment of Pharyngoesophageal Diverticulum by Inversion of the Sac. GEORGE CRILE, JR., and A. H. ROBNETT. *Cleveland Clin. Q.*, 1951, 18: 42.

A pharyngoesophageal diverticulum is composed of mucosa and submucosa herniating through the zone of the junction of the pharynx and esophagus and through the triangular space bounded by the fibers of the cricopharyngeal muscle and inferior constrictor muscles of the pharynx. The authors describe a method of treatment of this condition in which the sac is inverted. They allege cures in 11 consecutive cases which were followed for periods of 2 to 38 months. The technique is as follows:

Usually an incision is made over the anterior edge of the left sternocleidomastoid muscle from the level of the hyoid bone to the suprasternal notch. After retracting the muscles laterally and the thyroid medially, it is usually necessary to ligate the lateral thyroid vein and inferior thyroid artery. The recurrent laryngeal nerve is identified so that it can be avoided. The diverticulum is then grasped with smooth thumb forceps and dissected free until the neck is well mobilized. Inversion of the sac into the esophagus is accomplished by tightening a purse-string suture placed through the submucosa of the neck of the sac. Then, with an Ewald tube in the esophagus and the sac inverted, the defect between the cricopharyngeus and inferior constrictor muscles is closed with interrupted No. 60 cotton sutures. The platysma and fascia are closed without drainage, with No. 60 cotton, the skin edges are approximated with skin clips, and the Ewald tube is withdrawn.

Usually the patient is given an unrestricted diet by the fifth to the seventh postoperative day, and discharged.

JOHN J. BALLENGER, M.D.

NECK

Clinical Experiences in 21 Cases of Hyperparathyroidism, with Special Reference to the Prognosis Following Parathyroidectomy. JOHN HELLSTRÖM. *Acta chir., scand.*, 1950, 100: 391.

The author studied 21 cases of hyperparathyroidism (5 male and 16 female patients). Twelve of the patients were under observation for periods of from 5 to 20 years. Eighteen patients underwent parathyroidectomy; the extirpated parathyroid glands were classified as diffuse hyperplasia in 5 cases and as adenoma in the remaining 13 cases.

The prognosis following parathyroidectomy in hyperparathyroidism is chiefly dependent upon the degree of renal damage at the time of operation; the skeletal changes are of less importance. A certain improvement of the renal damage is possible after parathyroidectomy, but in most cases the damage is lasting, or even progressive. Evaluation of the prognosis calls for a long follow-up period of observation since the patients may be apparently healthy for many years but ultimately die from sequelae of hyperparathyroidism, even if the latter has been checked by parathyroidectomy.

Evidence of renal damage is an early symptom of hyperparathyroidism and is due mainly to calcium deposition in the tubular epithelium and to vascular changes leading to nephrosclerosis. Clinically, the renal damage is manifested at an early stage of the disease by impaired urinary concentration, resulting in polyuria and hyposthenuria.

In most cases of hyperparathyroidism there occurs a rise in blood pressure which in the early stages is of a more transitory nature, but which in due course of time becomes manifest and constitutes an important reason for the poor prognosis. Since early diagnosis and operation are factors determining the prognosis, the blood calcium and blood phosphorus levels should be investigated whenever symptoms are present that might conceivably be ascribed to hyperparathyroidism.

Parathyroidectomy is the only treatment; treatment by irradiation is ineffective and ill-advised. In adenoma it usually suffices to extirpate the involved parathyroid gland. In diffuse hyperplasia sufficient parathyroid tissue should be removed, if possible, to cure the hypercalcemia without giving rise to tetany; however, even partial parathyroidectomy, which does not lead to disappearance of the hyperparathyroidism, may nevertheless improve the patient's condition.

The pathogenesis of hyperparathyroidism is still unknown.

ROBERT TURELL, M.D.

Recent Developments in the Diagnosis of Thyrotoxicosis. JOHN HERTZ. *J. Internat. Coll. Surgeons*, 1950, 14: 653.

The author reviews the cardiac symptoms of thyrotoxicosis and calls attention to their importance in the diagnosis of this condition.

The increase in systolic, diastolic, and pulse pressure is discussed, as well as its disappearance after correction of the thyrotoxicosis. There is also a definite tachycardia with the disease. The author finds that the minute volume of the heart is increased because of the increase in cardiac rate and the increase in the systolic output of the heart.

Auricular fibrillation often accompanies toxic thyroid disease, as do other cardiac signs diagnosed only by electrocardiogram. One of these is the increase in the P wave. This was studied with relation to the

compression of the trachea, and the author believes it results from a reaction of the heart to the compression or dislocation of the trachea. There may also be alterations in the T waves as well as other electrocardiographic findings.

Increase in the width of the heart and prominence of the pulmonary arch are frequently demonstrable by x-ray examination in patients with thyrotoxicosis. These changes revert to normal in most patients after correction of the toxic state. It is emphasized that all of these cardiovascular findings are not contraindications to operation, but rather indicate its need.

The presence of exophthalmos in thyrotoxicosis is discussed, especially as regards its etiology. Increase in orbital contents, contraction of certain orbital muscles, and hypotonia of the extrabulbar orbital muscles are given as the main etiological theories of exophthalmos. Each of these theories is discussed. The author was able to find evidence of degenerative changes in the extrabulbar muscles, which confirms the views expressed by Rundle in his considerations. The cervical sympathetic system may play a part in this condition as well. The fact that the exophthalmos may completely disappear after operation is stressed.

The alterations in basal metabolism are discussed also, together with unusual forms of thyrotoxicosis.

It appears to be the author's opinion that the various cardiac symptoms play an important part in the clinical diagnosis of thyrotoxicosis.

DONALD C. GEIST, M.D.

Malignant Disease of the Thyroid. HUGH R. G. POATE. *Austral. N. Zealand J. Surg.*, 1950, 20: 114.

Carcinoma of the thyroid gland exhibits several peculiarities, compared with carcinoma in general. It knows no age limitation, and most often arises in a lesion that, apparently, has been benign for most of the patient's lifetime. Moreover, it is frequently compatible with a long period of life even in the presence of metastases in the lungs or bony skeleton. At the opposite extreme, malignant disease of the thyroid gland may cause death within a few months.

Carcinoma of the thyroid gland is seldom found in association with acute thyrotoxicosis; however, Pemberton and Black, in a collected series of 1,310 cases of carcinoma of the thyroid gland, found a 1.75 per cent incidence of carcinoma associated with exophthalmic goiter. It is interesting to note that in many cases of carcinoma of the thyroid gland there may be some elevation of the basal metabolic rate along with symptoms of a low grade thyrotoxicosis. This probably results from hyperfunction due to hyperplasia in the benign tissue of the gland rather than in the malignant tissue.

Recent and progressive development of a single nodule, especially in middle life, should be regarded with suspicion. Acute swelling in a pre-existing nodule, with pain and tenderness suggesting hemorrhage into the tumor, is likely to be of grave import, especially in patients over 50 years of age. A single mass in one lobe of the thyroid gland, irrespective of the age of the patient, is also to be regarded with suspicion, particularly in a male, since carcinoma is about twice as common in the male as compared with similar tumors in the female. There is general agreement that all discrete nodules require operation, irrespective of the age of the patient.

The use of frozen sections in the laboratory as a method of diagnosis of malignant disease has proved quite unreliable. If there is any reasonable doubt, the lesion should be regarded as malignant and a radical operation undertaken. The only type of carcinoma which is readily recognizable is the papillary variety which occurs in relatively young people and is characterized usually by multiple metastases to the cervical lymph nodes. These were formerly considered as tumors in lateral aberrant thyroid tissue, but it is now generally agreed that a primary focus can always be found in the thyroid gland.

ORVILLE F. GRIMES, M.D.

Bilateral Thyrotomy for Carcinoma of the Larynx. JOSEPH I. KEMLER. *N. England J. M.*, 1951, 244: 275.

The indication for bilateral thyrotomy for carcinoma of the larynx has been established: namely, a carcinoma situated in the anterior two-thirds of the larynx limited to one cord and without its fixation. Some authors advocate this operation even if the disease has spread across the anterior commissure so that all of one cord and a portion of the other cord must be excised. Since carcinoma of the larynx is mostly found in the anterior part of the larynx and is of the squamous type, it destroys by direct extension, rather than by metastasis. Although the cartilages are highly resistant to the invasion of the carcinoma, there are two weak spots through which the new growth may spread either by direct extension or through migrating cells from the nearby growth. Another weak point, the cricothyroid membrane should also be removed. The classic laryngofissure, the simple or anterior commissure operation, cuts the cartilage in the midline where cancer cells may be present. It is difficult to separate the inner perichondrium, with tumor tissue possibly present in the anterior commissure, from the cartilage without tearing. The more posteriorly inner perichondrium is easily separated. To take advantage of this factor, and to eliminate the danger of carcinomatous spread through the anterior commissure, the bilateral thyrotomy for carcinoma of the larynx was devised. By this operation, the anterior commissure with cartilage attached, part of the uninvolved cord, the old involved cord and arytenoid cartilage, if necessary, and the cricothyroid membrane are removed in one mass. The technique of this operation is illustrated in Figures 1 and 2.

The operation cannot be recommended for women because the anteroposterior diameter of their larynx is rather short and the breathing space may not be adequate after the anterior commissure is taken

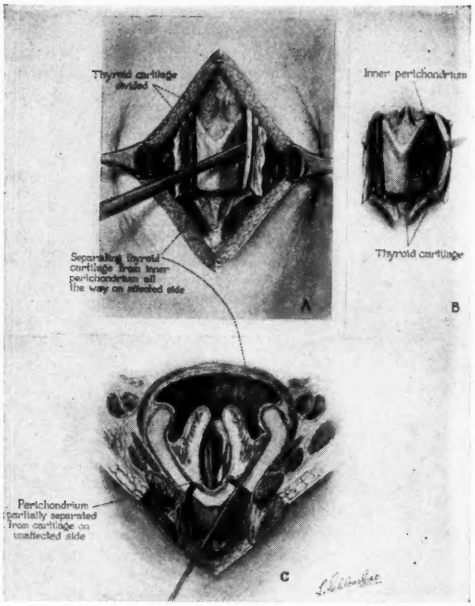

Fig. 1. (Kemler)

out. The author has operated on 15 men patients with uniformly good results. Bilateral thyrotomy can be used only on tumors requiring laryngofissure and also in more advanced cases of carcinoma of the larynx, provided that the tumor can still be removed with an ample margin of normal tissue. The defect is filled in by newly formed healthy tissues which compensates for the loss of the whole cord. There is ample room for breathing and the formation is as good as it is after any laryngofissure operation. All the patients so operated on are still under observation by the author.

The advantages of the operation are: (1) short incision, without dissection of the flaps and without interference with the thyroid gland, (2) ease of cutting the cartilages without injuring the inner perichondrium, (3) ease of dissection of the inner perichondrium without danger of cutting the tumor or cutting too close to it, (4) removal of the crista, with the anterior commissure and with the cord or cords, (5) minimum manipulation after opening of the larynx, (6) no need of a tracheotomy tube, (7) good exposure with least retraction of cartilages, (8) more thorough extirpation of the tumor with a good deal of surrounding tissue en masse without mutilation, (9) easy control of bleeding, (10) rapid healing, with little or no reaction, (11) small risk of stenosis, as the cartilages have a tendency to spread apart rather than to collapse, and (12) effectiveness of this method in all cases of carcinoma of the larynx in men suitable for laryngofissural or anterior commissural operations. In many cases this procedure may take the place of laryngectomy.

JOHN E. KARABIN, M.D.

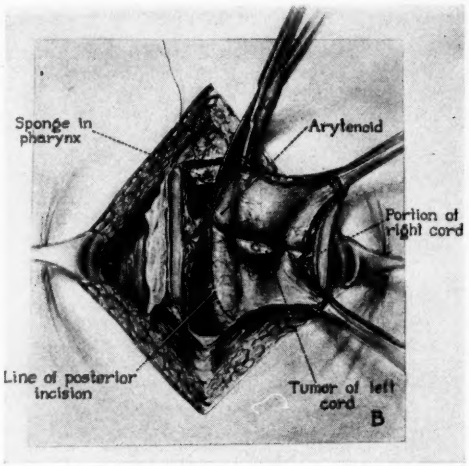

Fig. 2. (Kemler)

Tracheotomy after Thyroidectomy. FRANK H. LAHEY and WALTER B. HOOVER. *Ann. Surg.*, 1951, 133: 65.

There are four conditions associated with, and following, thyroidectomy that may require tracheotomy: (1) postoperative edema of the larynx; (2) postoperative accumulation of blood beneath the muscle flaps, usually the result of arterial hemorrhage either from the inferior thyroid artery or the superior thyroid artery (the postoperative venous oozing either beneath the muscle flaps or beneath the skin flaps); (3) the narrowed trachea from intrathoracic or partly intrathoracic goiter in which there is doubt as to whether the patient will be able to get enough air immediately after operation; and (4) the deliberate tracheotomy at the time of operation done upon patients with cancer of the thyroid as a precaution against the compression of the trachea which will follow the reaction and the swelling after high voltage x-radiation which is employed postoperatively in these cases. It is pointed out by the author, in discussing the indications for tracheotomy in the first and second groups of patients, that it is impossible to state specifically just when tracheotomy should be done. In the first group, laryngeal edema is deceptively slow and possessed of no compelling features such as are found in the active hemorrhage group. It is the first group of cases, the laryngeal edema group, that has given the greatest concern. It is the authors' belief that the time to do a tracheotomy in these cases, or to re-open the wound to relieve pressure in postthyroidectomy patients with breath-

ing difficulty, is when one begins to wonder whether or not he should do it. It is true that this rule may promote doing more tracheotomies and wound re-openings, but the author would prefer this position since it leaves us with live patients.

In the second group of postthyroidectomy patients in whom the decision for or against tracheotomy must be made, particularly those in whom the respiratory obstruction is brought about by the occurrence of arterial hemorrhage (superior or inferior thyroid artery) beneath the prethyroid muscle layer, sternohyoid, and sternothyroid, the decision is much more easily made because of the rapidity with which the obstruction occurs and because of the completeness of its character. It is a decision about which there can be less delay and often one which must be made in terms of minutes. The obstruction in the cases in this group is so complete that the decision will not be so much whether or not it should be done but whether or not it can be done in time. The diminishing adequate state of oxygen exchange is very obvious in the patient. One can palpate the neck in these cases and observe a distinct sense of firmness of the front of the neck with a forward projection of the muscles and skin flaps due to the accumulation of blood beneath the muscle flaps; a distinct forward tension of the sutured prethyroid muscle flaps can be felt also. The relief of pressure by opening the wound and removing clots supersedes asepsis and must be done promptly as a life-saving procedure. In order to minimize postthyroidectomy arterial hemorrhage, several technical points have been suggested. The first point is that after subtotal thyroidectomy is completed, the stump of the superior thyroid artery, is retired for a second time at a higher level than where it had been previously ligated and cut. The other warning is that ligation of the inferior thyroid artery must be done without cutting beyond the ligature. If the inferior thyroid artery for any reason requires cutting, one should, as in the superior thyroid artery, apply a second protective tie well beyond the original ligature.

The third type of tracheal obstruction is that in the patient with an intrathoracic or partly intrathoracic thyroid in whom a marked degree of tracheal narrowing has occurred. There is the occasional case in which, because of an associated hyperthyroidism together with retardation of the action of the vocal cords and the expected degree of edema of the larynx secondary to the removal of such an intrathoracic goiter, there is a question whether or not the patient would have adequate intake of air after operation. Thus, the combination of factors, such as marked narrowing of the trachea, retardation of cord action, increasing tracheal pressure, and the need for immediate removal of the intrathoracic adenoma because of these symptoms before the secondary hyperthyroidism can be controlled, is an indication for tracheotomy and such a case is illustrated by the author. If there is any

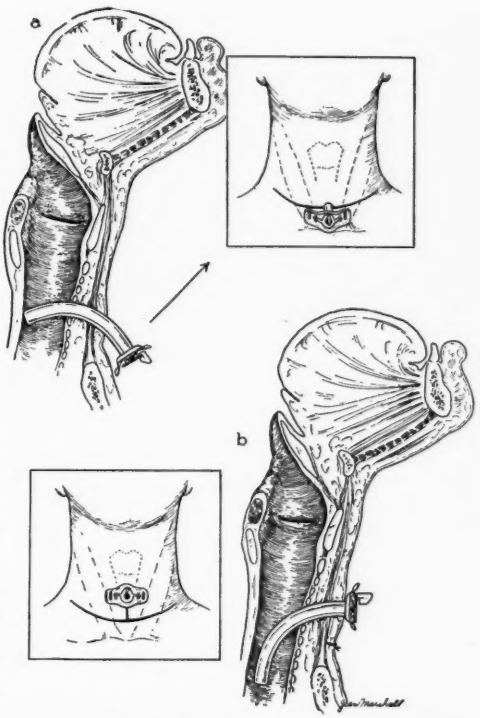

Fig. 1 (Lahey, Hoover). For purposes of better illustration in *a* is shown diagrammatically the improperly placed tube and in *b* the properly placed tube through a longitudinal incision in the scar.

serious doubt as to the ability of the patient to obtain an adequate intake of air postoperatively, a deliberate tracheotomy is done at the time of the subtotal thyroidectomy, rather than permitting the patient to go through the hazards of a postthyroidectomy tracheotomy when the risk is infinitely greater. Tracheotomy done in the patients with extensive cancer of the thyroid gland involving both lobes is discussed. The tracheotomy is not a problem in early carcinoma of the thyroid involving but one lobe or a part of a lobe, but it does arise in patients with advanced carcinoma of the thyroid, because if one attempts to irradiate a bilateral thyroid cancer with the trachea unexposed, the postoperative reaction, and the edema and compression of the trachea will require an emergency tracheotomy through the unremoved malignant thyroid tissue over the isthmus. In these cases the entire lobe on one side together with the entire isthmus is removed, the trachea is completely bared, and then a tracheotomy is performed. Thus, any degree of roentgen therapy can be carried on safely without the danger of obstruction to breathing. In the

authors' experience a total thyroidectomy in advanced carcinoma has not been advisable because frequently the tumor extends into the mediastinum and is frequently fused with the trachea, and in many cases the surgical procedure would result in tetany with bilateral abductor paralysis and even esophageal fistula in some cases. Another warning presented concerns the patients with unilateral abductor paralysis from previous thyroid surgery, in whom the glottic space has been materially cut down. A much closer watch must be kept on these patients for the possible need for tracheotomy than on those whose cords are functioning normally because a small amount of edema can diminish or narrow the glottic space so that a tracheotomy would frequently be necessary.

The tracheotomy should be done at least below the first ring of the trachea or, even better, below the second tracheal ring or lower. The cricoid cartilage should not be in contact with the tracheotomy tube because of the danger of infiltration and edema which may extend along the larynx; even contact with a part of the basic cartilage of the larynx may cause a cicatricial stricture of the larynx that may make permanent removal of the tube impossible. The tracheal opening for the tracheotomy tube must be at a lower level than the opening in the skin through which the tube must pass. A poor position of the tracheal tube interferes with the airway and produces undesirable ulceration and irritation of the tracheal wall (Fig. 1). The tracheotomy tube should be of adequate size and length, and if there is any question as to whether the tube reaches below the level of the tracheal obstruction, checking its position by roentgenologic examination of the trachea will often give the necessary information.

At the time of the tracheotomy, a drain of gauze is placed about the tracheotomy tube from the tracheal opening to the skin surface, and the wound is closed about the tracheotomy tube. The regular removal of secretions from the tube and the trachea is most important in the postoperative care of the tracheotomized patient.

The removal of the tracheotomy tube may be done as soon as the adequate airway of the larynx and trachea has been re-established. This may be tested by plugging the tracheotomy tube for a short time, and if the patient is comfortable and can sleep with the tube plugged, it may be assumed there is an adequate airway.

JOHN E. KARABIN, M.D.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Ventriculo-Cisterno-Stomia of Torkildsen in the Treatment of Obstructive Hydrocephalus (Sulla ventriculo-cisterno-stomia di Torkildsen nel trattamento degli idrocefali ostruttivi). G. M. FASIANI and M. QUARTI-TREVANO. *Chirurgia*, Milano, 1950, 5: 81.

Thirty-seven Torkildsen operations were done for obstructive hydrocephalus at the general surgical clinic of the University of Milan, Italy, during the past 3 years. During this period the operation of Stookey and Scarff (direct ventriculocisternostomy) was selected for this indication in 80 instances. The Stookey and Scarff method was preferred when the obstruction was situated at the posterior end of the third ventricle, or even further back, especially in those instances in which the dilated (hydrocephalic) ventricular cavity bulged backward as a thin sac. The Torkildsen method was also preferred in those cases in which the obstruction was situated far forward, in other words, in those cases in which there seemed to be no other means of obtaining adequate drainage from the blocked ventricles.

The technique employed by the authors is adequately portrayed in Figure 1. The tube used for drainage, which passes indirectly from the ventricle to the cisterna magna beneath the cerebellum, is of rubber. It is carried in a groove cut in the outer surface of the squama occipitalis and re-enters the cerebrospinal cavity just beneath the foramen magnum; it may be necessary to sacrifice the posterior arc of the atlas in short-necked, muscular individuals.

When the obstruction is so far forward as to actually isolate the two lateral ventricles the authors prefer, instead of repeating the operation bilaterally, to connect the unoperated ventricle with the other in a similar manner. This procedure is adequately shown in Figure 2.

Of the 37 patients operated upon by the method of Torkildsen, 10 died in the first few days following the operation (operative mortality 33 per cent). Three of these died of postoperative hemorrhage, 2 from the tumor itself. Those who survived the operation have, on the whole, done well. In the cases in which the tumor was irremovable the operation was, of course, followed by adequate roentgen therapy. Of the first 17 patients operated upon, 5 died from the operation. Of the 12 survivors, 2 died 6 and 8 months later, respectively. The remaining 10 are still living after 32, 24, 21, 20, 19, 17, 14, and 12 months, respectively. These have in large measure returned to their former occupations.

The value of this small group of patients lies in the fact that they comprise a homogeneous series, composed almost exclusively of conditions of obstruction of the third ventricle and all except one patient had an obstruction caused by tumor development in the walls of the ventricle, occluding the ventricular cavity completely, or almost completely.

From these experiences the authors conclude that the indirect ventriculocisternostomy of Tor-

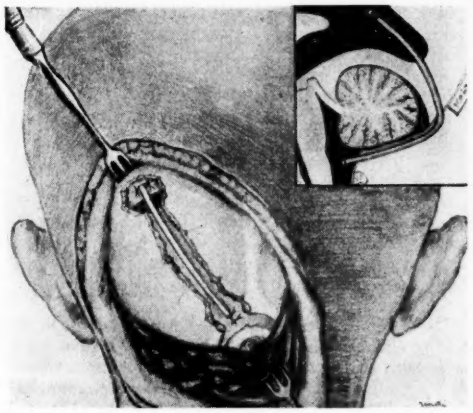

Fig. 1 (Fasiani and Quarti-Trevano).

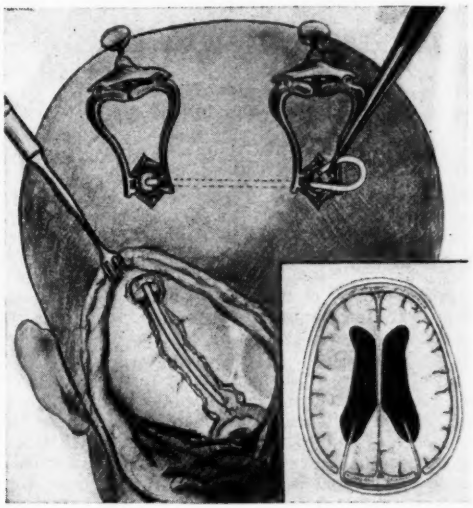

Fig. 2

kildsen is able to provide efficacious drainage of the cerebral cavities in those instances in which the ventriculostomy of the third ventricle cannot be applied. JOHN W. BRENNAN, M.D.

Radioactive Diiodofluorescein in Diagnosis and Localization of Central Nervous System Tumors. LOYAL DAVIS, JOHN MARTIN, MOSES ASHKENAZY, GEORGE V. LEROY, and THEODORE FIELDS. *J. Am. M. Ass.*, 1950, 144: 1424.

At the time this article was written, the authors had studied 200 patients with the presumptive diagnosis of a space-occupying lesion of the central nervous system, and a new technique was used which employs the intravenous administration of the radioactive dye, diiodofluorescein. In all patients the results of the radio-dye tests were compared with those obtained using the ordinary clinical means of diagnosis, electroencephalography, pneumoencephalography, and in some instances angiography as well. In every patient the absolute diagnosis was verified by surgical operation or at autopsy (or both), and a microscopic study of the diseased tissue was made.

Stable radioactive diiodofluorescein in a dosage of 1.1 millicuries is injected intravenously, using appropriate radioisotope precautions to prevent contamination of the skin of the patient and operator. The uptake of the dye by the brain is then determined by external counting with the aid of a single channel differential radiation localizer. A properly shielded small Geiger-Mueller tube, a modified general radio counting rate meter with a 1,000 count per minute full scale range (connected to the tube through a preamplifier), and a mechanical graphic recorder with a recording speed of 6 minutes per inch, are the essential parts of the apparatus. Thirty-two positions on the head, on and above Reid's base line (13 positions on either side of the head and 6 positions for midline readings) are studied over a four hour period with the tube in place at each location for 3 minutes, symmetrical areas being studied consecutively. The increase in counts per minute are directly recorded, and can be directly compared with well established predetermined "normal" rates found in the study of a series of normal brains.

In the series of 200 patients, practically all the common space-occupying lesions of the brain were encountered, so that there was ample opportunity to learn the radio-dye characteristics of the various primary tumors of the brain, tumors of the blood vessels, meningiomas, hypophyseal tumors, acoustic neurinomas, metastatic tumors, abscesses, hematomas, and cysts.

The accuracy of the test was particularly gratifying in that it was found to focalize the lesion, and not merely place it in one hemisphere or the other. In fact, it was found to be 95 per cent accurate in those patients actually eventually proved to have a space-occupying lesion, as compared to 63 per cent for pneumography and only 45 per cent for electroencephalography, so far as focal placement of the lesion was concerned. Since the degree of uptake is determined by the degree of capillary change due to proliferating tumor cells, the readings were higher over the more vascular, more malignant, and cellular tumors, less active over indolent tumors such as partially calcified oligodendrogliomas and astrocytomas, and actually less than normal over degenerated, cystic, or necrotic areas.

The negative results also proved to be approximately 95 per cent accurate, and were of importance in the differential diagnosis of cerebral neoplasms from such lesions as hypertensive cerebrovascular accidents, perichiasmal arachnoiditis, intracranial aneurysms, and meningovascular syphilis. The test was useful for the localization of tumors in the cervical and lower lumbosacral vertebral canal, but less useful for tumors in the thoracic region of the cord, because of the concurrent radiations of gamma waves from the lungs, spleen, liver, and the intestines.

The test offers a safe, painless, and reliable method for the localization of intracranial tumors, and with the further development of instrumentation and technique it should grow into a valuable diagnostic aid. JOHN MARTIN, M.D.

SPINAL CORD AND ITS COVERINGS

Orthopedic Signs in the Diagnosis of Disc Protrusion, with Special Reference to the Straight Leg Raising Test. JOHN CHARNLEY. *Lancet*, Lond., 1951, 260: 186.

This article concerns several investigative procedures in regard to the lumbar spine, directly and indirectly related with the intervertebral disc. The author studied the isolated lumbar vertebra and measurements revealed that the "bending axis" of the spine lies about 5 mm. anterior to the front surface of the spinal theca, which is somewhere in the posterior quarter of the intervertebral disc. Other studies on possible movement and elasticity of the spinal dura and nerve roots revealed that the anterior aspect of the dura is closely connected with the posterior surfaces of the vertebral body and the greatest movement between flexion and extension is only 5 mm. over the entire lumbar vertebra. The posterior aspect of the dura, however, is covered by epidural fat and could change a distance of 11 mm. The normal dura is never stretched beyond its maximum length.

It is believed that flattening of the lumbar spine, or lumber kyphosis with sciatica is not a reflex mechanism to reduce tension or pressure on the nerve root but that it is "most probably a primary deformity of the lumbar spine resulting directly from altered disc mechanics."

The more important aspect of this study is in regard to the straight leg raising test. The author believes that the straight leg raising test is more valuable than all other clinical or radiological signs combined in the diagnosis and prognosis following surgery on patients with herniated intervertebral disc.

The author has studied 88 patients. Ninety-two per cent of these, with definite limitation of straight leg raising to less than 40 degrees, revealed a protruded disc. In 25 patients with less limitation in straight leg raising, only 64 per cent had a protruded disc. Likewise, it was found that a remarkably high percentage of the patients who received excellent results by surgery upon the disc were among those with marked limitation of straight leg raising.

In the author's opinion, straight leg raising limited to less than 40 degrees indicates the movement of the nerve root against a protruded disc; whereas, where straight leg raising is only slightly limited, that is, to about 70 or 80 degrees, the pain "is caused by the start of tension on a root which is abnormally sensitive, from causes intrinsic to the root, and not necessarily accompanied by a demonstrable lesion of an intervertebral disc." JACK I. WOOLF, M.D.

SYMPATHETIC NERVES

Regeneration of the Cervical Sympathetic. A. R. C. BUTSON. *Brit. J. Surg.*, 1950, 38: 223.

The author presents the results of his investigations to provide experimental evidence concerning the rate of regeneration of preganglionic fibers by interrupting the cervical sympathetic trunk and noting the time of return of function of the eye structures involved, and the correlated histologic changes in the nerve.

Adult rabbits of both sexes were used. Lesions of the cervical sympathetic trunk were created by (a) crushing the nerve trunk, (b) simple section of the trunk, (c) excision of a portion of the trunk, (d) section of the postganglionic fibers from the superior cervical ganglion, and (e) excision of the superior cervical ganglion. Observations on the return of function of the eye, and histologic studies of the nerve regeneration after crushing were then made. The latter included determining the number of medullated fibers as well as the maturation of the medullated fibers.

Similar studies were carried out on adult cats of both sexes. In these experiments, the lesions were created by (a) crushing, (b) simple section of the nerve, and (c) resection of a portion of the nerve. The same observations as those made in the rabbit series were then recorded.

A marked species difference was noted in comparing the two series. The period of delay before return of function begins is considerably less in cats than in rabbits. The advance of functional recovery is also faster in cats than in rabbits. Experiments on the effect of gaps in the sympathetic trunks showed the cat to be capable of more regenerative power than the rabbit. The results of the histologic study of the medullated and nonmedullated fibers were very similar in the 2 animals.

DONALD C. GEIST, M.D.

MISCELLANEOUS

The Relative Merits of Various Suture Materials for the Repair of Severed Nerves. S. SUNDERLAND and G. K. SMITH. *Austral. N. Zealand J. Surg.*, 1950, 20: 85.

Despite a number of earlier experiments on tissue reactions about various suture materials used in the repair of peripheral nerves, there has usually been a failure to carefully evaluate and differentiate the reaction due to the injury and those which would occur in the natural process of healing. Hence the authors have performed each experiment with a control in which the identical procedure of suturing the nerve was carried out but the suture material was not left *in situ*.

Two distinct types of tissue reaction were found. One was a cellular reaction consisting of polymorphonuclear leucocytes, lymphocytes, histiocytes, giant cells and, in the case of silk, plasma cells. This reaction is maximal in the early stages and is not especially harmful to the regenerating axons. On this basis alone, the various suture materials used were graded from the most favorable to the least favorable, as follows: tantalum, human hair, nylon, plain catgut, silk, and chromic catgut.

The second type of tissue reaction was mainly a fibroblastic activity which usually occurred in the later stages and was directed mainly toward an attempt to seal off the more permanent foreign body sutures. Since the fibroblasts result in greater scar tissue and hence constrict the regenerating fibers, it is felt that this is by far the least desirable reaction. On this basis the suture materials giving the least fibroblastic reaction are arranged in the following order of priority: plain catgut, chromic catgut and silk, human hair, tantalum, and nylon. It is realized that certain technical factors are also of great importance, and in considering the tensile strength and ease of application of the suture materials as weighed against the possible tissue reaction, it is believed that silk has a slight advantage over plain catgut when all factors are taken into consideration. However, fine plain catgut is still preferable to all of the other nonabsorbable suture materials used. "The outcome following nerve suture does not depend solely on the type of suture material employed but to a large degree on the manner in which it is used to unite the nerve ends."

JACK I. WOOLF, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Cartilaginous Tumors of Ribs and Sternum. Lawrence W. O'Neal and Lauren V. Ackerman. *J. Thorac. Surg.*, 1951, 21: 71.

Because cartilaginous tumors of the ribs and sternum are prone to malignancy and because the differentiation between benign and malignant cannot be made with certainty, O'Neal and Ackerman believe that adequate radical resection of the ribs and sternum with removal of long segments of the bone of origin, the periosteum, adjacent muscle, underlying pleura, and adjacent bony structure, is imperative.

The authors summarize 85 of the reported cases and add 11 more of their own, making a total of 96 reported cases in the literature. These tumors fit the histologic diagnosis of malignancy in cartilaginous tumors, as established by Jaffe and Lichtenstein. The tumor may be single or multiple, and too much dependence cannot be placed on roentgen examination as great difficulty is experienced in obtaining adequate views, particularly in small tumors of the sternum and those at the extreme anterior ends of ribs. In doubtful cases, aspiration or incisional biopsy is believed to be in order. Poor results from the treatment may be traced to a tendency to surgical conservatism because of lack of a true appreciation of their nature. Stephen A. Zieman, M.D.

Papillary Neoplasms of the Breast. C. D. Haagensen, Arthur Purdy Stout, and Jim S. Phillips. *Ann. Surg.*, 1951, 133: 18.

There are two main types of papillary neoplasms of the breast: benign intraductal papillomas, which are relatively frequent, and malignant papillary carcinomas, which are rare. Both types give rise to serous or bloody discharge from the nipple. The present article concerns benign intraductal papillomas. The material is from the Presbyterian Hospital, New York, and the Laboratory of Surgical Pathology of the College of Physicians and Surgeons. The authors believe that the lesion is benign and that there has been a tendency to employ a comparatively radical method of treatment. Their studies covered the period from 1916 to 1941, and records of 353 cases were used. The lesions were divided into two types: those presenting a mass clinically and those discovered on microscopic study. In this condition, one or more papillomas grow within a duct and attain sufficient size to fill the duct. The delicate projections break off or are damaged, and serous or bloody fluid escapes. In many cases the mass is not palpable, while in others there is a radial linear thickening beneath or adjacent to the aureola. The growths are situated near the nipple in the larger ducts.

The microscopic papillomas do not constitute a separate disease entity. They are a manifestation of the protean lesion which is called cystic mastitis. They may be found in any portion of the breast and rarely, if ever, produce nipple discharge.

Ages of the patients in this series range from 19 to 82. The mean age incidence was somewhat younger than that of patients with breast carcinoma. Eighty-six per cent of central tumors as compared with only 29 per cent of peripheral tumors had a sanguineous or serous discharge. The discharge was serous in 23 cases and bloody in 55 cases. There were intervals without discharge in some patients. It was found that the more solid glandular type of papillary disease in which a discharge is less frequent was more commonly located in the periphery of the breast. Highly papillary growths were more in the central portion of the breast. A tumor was present in almost all of the early cases. Today, intraductal papillomas are diagnosed without the presence of a tumor.

The tumors range in size from 0.3 cm. to 10.5 cm. Most of them measured only 3 or 4 mm. in diameter and extended along the duct for 1 or 2 cm. In rare cases, the papilloma is in the portion of the duct traversing the nipple. This condition is usually of long duration. In 11 cases the tumor had been present for 10 years or more, and in 8 cases for 5 years or more. The discharge may be recurrent with long intervals of freedom from discharge. Some patients find that pressure over the lump expresses the discharge and relieves the discomfort. Involvement of both breasts sometimes occurs.

The proliferated epithelial cells are supported upon vascular stalks which may be thin or broad. Scarring sometimes forms, giving the false impression of glandlike tubes and infiltrative growth. In benign growths, the cells resemble normal duct epithelium, but it must be remembered that normal duct cells vary considerably. In doubtful cases the decision generally rests upon the nucleus; if this has the appearance of anaplasia with hyperchromatism, accentuation of the chromatin network or large nucleoli, and particularly if there are more than rare, widely separated mitoses, the growth can safely be considered cancer. In the authors' experience, solitary nodules of papillary carcinoma almost never show traces of benign intraductal proliferations, so that in doubtful cases, if there are microscopic cells which one might be tempted to consider cancerous within an otherwise benign papillary tumor, the technique elsewhere described for the local excision of benign papillomas will also cure such tumors. Either these cells are not cancer cells, or, if one chooses to regard them as such, the condition is comparable to cancer *in situ*. Treatment varied considerably, depending upon the surgeon. The authors stress the importance of study of permanent sections in this condition rather than using the frozen section technique. The delay is overshadowed by the importance of accurate study.

It is believed that the best results are obtained when a correct clinical diagnosis is made and the approximate site is determined. A circumareolar incision was made which permitted a flap to be turned back to the base of the nipple. The diseased duct was then identified and dissected out, cut off at the base of the nipple, and traced distally until the papilloma within it was found. The diseased duct, or ducts, together with a wedge-shaped sector of the surrounding breast tissue were then excised. This is thought to be the ideal therapy.

Seventy-two patients with local excision were followed; of these, 3 had recurrences; in none of the patients had carcinoma developed.

The dissection must be meticulous with careful control of bleeding, and accurate identification of the papilloma; a wedge-shaped sector of surrounding breast tissue should be excised. The authors believe that there should be less confusion among pathologists in distinguishing benign papilloma from papillary carcinoma; papillary carcinomas are very rare.

Even if the lesion proves to be a papillary carcinoma, delay caused by thorough study and consultation will not impair the chance of cure because the growth vigor of papillary carcinoma is decidedly less than that of ordinary breast carcinoma.

A patient with bloody or serous discharge, and no palpable tumor, can safely be assured of having no carcinoma. Such a patient is examined at frequent intervals, and in most cases a tumor is palpated after several examinations. The authors see no justification for recommending simple mastectomy for intraductal papilloma.

ROBERT E. FLORER, M.D.

Carcinoma Mammae Latens. JERZY RUTKOWSKI. *J. internat. chir.*, Brux., 1950, 10: 415.

The author reviews 5 personal cases, and 3 cases observed by another author, in which carcinoma of the breast was characterized by axillary or supraclavicular metastases in the absence of a demonstrable primary site in the breast. He has called this "carcinoma mammae latens." The pathologist was sometimes able to demonstrate a small primary lesion following excision of the breast.

Because of the rapidly fatal outcome of these cases, radical mastectomy should be done as soon as the metastasis is identified. ROBERT L. CRAIG, M.D.

TRACHEA, LUNGS, AND PLEURA

Single, Circumscribed, Intrathoracic Densities. HANS ABELES and DAVID EHRLICH. *N. England J. M.*, 1951, 244: 85.

Without attempting to determine the incidence of single, circumscribed, intrathoracic densities in this communication, the authors have analyzed 44 cases found by mass x-ray surveys.

Despite careful study by various clinical and laboratory methods, it could not be determined whether this lesion was benign or malignant. In 21 cases (48%), exploratory thoracotomy was advised and the following conditions were revealed: primary carcinoma of lung in 5 cases; metastatic carcinoma of lung in 1, fibrosarcoma of pleura in 1, thymoma in 1, neurofibroma of lung in 1, adenoma in 1, and chondroma in 1 case each; tuberculoma in 5 cases; chronic lung abscess in 2 cases; bronchiectatic cyst in 1, lipoid pneumonia in 1, and pericardial cyst in 1 case each.

In 13 patients (30%) periodic examination was advised because evidence pointed to diseases other than malignancy. In none of these patients did any malignant changes develop during the follow-up of at least 2 years.

In 10 additional cases (22%), malignant disease could not be ruled out, and surgery was advised but not done. Six of these patients were advised against immediate surgery by their family physicians, mainly because they were asymptomatic. In a year or more the lesions in 5 of these cases developed into advanced carcinoma, in 3 cases the lesions have shown no change in size, and in 2 cases the lesions have increased in size over a period of 18 months but have remained stationary in the following 18 months.

In this series, 30 per cent of single, circumscribed, intrathoracic densities were found to be malignant. The tests used, and the difficulty experienced in trying to make a preoperative diagnosis are discussed. ROBERT L. CRAIG, M.D.

Nonspecific Pneumonitis of the Left Upper Lobe (Simulating the "Middle Lobe Syndrome" and Producing an Early Superior Pulmonary Sulcus Syndrome). WILLIAM M. ASHE, JOHN R. MCDONALD, and O. THERON CLAGETT. *J. Thorac. Surg.*, 1951, 21: 1.

The authors' report deals with a case in which nonspecific pneumonitis was situated in the apex of the left upper lobe. The lesion produced some symptoms characteristic of the superior pulmonary sulcus syndrome, and the pathologic findings in the resected left upper lobe resembled those of the so-called middle lobe syndrome reported by Graham, Burford, and Mayer as a disease entity.

Pancoast's conclusions concerning the syndrome bearing his name are well known. This syndrome has since been known by various names, and it has been established by numerous authors that any tumor situated in the region of the thoracic inlet will likely produce the characteristic symptom complex of involvement of the brachial plexus and the cervical sympathetic chain, and that bone will be involved as the mass enlarges and infiltrates. Herbut and Watson reported 17 cases which they had observed. All features of the syndrome were not present in each individual case, but these authors said that the disease had been universally due to a malignant lesion and had always proved fatal.

It therefore was of interest to Ashe, McDonald, and Clagett to report a case in which a benign lesion of the upper lobe of the left lung produced early changes characteristic of a superior pulmonary sul-

cus tumor (Pancoast's syndrome). They believe that the short duration of the patient's illness, before resection of the left upper lobe was performed, accounted for the absence of the more serious symptoms and signs of the superior pulmonary sulcus syndrome. It was also of interest that the pathologic examination of the excised lobe in some ways resembled the picture of the so-called middle lobe syndrome.

The excised upper lobe of the left lung in the case reported contained enlarged, firm lymph nodes which encircled the left main bronchus and left upper lobe bronchus. These nodes produced no extrinsic compression of the bronchus, endobronchial stenosis, or bronchiectatic changes in the upper lobe of the left lung. The pathologic changes in the involved parenchyma of the lobe were typically those of a nonspecific inflammatory pneumonitis. It is suggested that the term "middle lobe syndrome" does not represent a distinct entity of a middle lobe "atelectasis" but that the same pathologic picture may be produced elsewhere in the lungs, without bronchial stenosis and the bronchiectatic changes of obstructive pneumonitis.

Unusual Conditions Simulating Pulmonary Atelectasis with Case Reports of Agenesis and Hypoplasia of the Lung and of Fracture of the Bronchus, Together with Report of a Case of Massive Atelectasis in Bronchial Asthma, Included for Comparison. ROBERT E. PRIEST. *Ann. Otol. Rhinol.*, 1950, 59: 889.

Six cases in which pulmonary atelectasis was the initial or working diagnosis are discussed. Five of these are unusual since, on further study, the condition in each patient proved to be one of the following: idiopathic pulmonary hypoplasia, pulmonary hypoplasia accompanying diaphragmatic hernia, unilateral pulmonary agenesis, and traumatic bronchial rupture. The sixth case of total pulmonary atelectasis, due to bronchial asthma, is included for comparison. Bronchoscopy was of material assistance in the diagnosis in all of these cases, and bronchography with the use of lipiodol was helpful in some.

W. FOSTER MONTGOMERY, M.D.

The Surgical Treatment of Bronchial Asthma. P. NYST. *Arch. chir. Neerl.*, 1950, 2: 261.

The author discusses at length the anatomy of innervation of the lung and the physiology of respiration. He mentions the theory of Pitt in which there are considered to be three respiratory centers in the pons and the medulla oblongata: (1) the inspiration center, (2) the expiration center; and (3) the pneumotactic center.

Sympathetic and parasympathetic nerves of a normal person are in equilibrium in the pulmonary system. In a pathologic condition, as in bronchial asthma, the balance is disturbed. Among the arguments in favor of reflex bronchial constrictions is the incidence of bronchospasms following mechanical stimulation of trigger areas situated in the region of the fifth, ninth, and tenth cerebral nerve centers.

The first surgical attack upon bronchial asthma was made in 1923 by Kuemmel, who performed a cervical sympathectomy. The history of this type of therapy is discussed down to 1938, at which time Rienhoff and Gay performed a resection of the posterior pulmonary plexus for the first time in a human. These authors assumed that the presence of bronchodilators in a human being has not yet been proved, and that if they do exist they are overshadowed by the bronchoconstrictors. The vagal and sympathetic nerves are blended, due to anastomoses in the cervical region. The imbalance of the autonomic nervous system is especially prominent in patients with a labile psychological reaction.

The author refers to the technique described by Alton Ochsner in 1946. By way of the fourth intercostal space on the right, the posterior pulmonary plexus is approached at the back of the hilum of the lung. The fifth intercostal space is used on the left. After the vagus has been freed, the branches to the hilum are resected to the extent of at least 1 cm. In 4 cases, the author removed the second to fifth thoracic ganglia. He operated on 11 patients suffering from intractable bronchial asthma during the period from November, 1946 to August, 1948. There were no complications during or after the operations. The results were as follows: very good in 1 case, much improved in 3 cases, not much improved in 3 cases, unchanged in 3 cases, and worse in 1 case. Only the afferent tracts of the vagus are interrupted in the lung tissue, and no postoperative subjective ill effects were demonstrated.

The author states that surgical treatment of bronchial asthma is indicated when internal therapy has failed or when serious invalidism or death seem inevitable. The relative indications are: when the spastic complex of symptoms becomes prominent, or is induced by irritation of trigger areas extraneous to the deep air passages; and when infection and emphysema (fixed type) do not dominate.

ROBERT E. FLORER, M.D.

Resection Versus Thoracoplasty in the Treatment of Pulmonary Tuberculosis. ARCH. J. BEATTY, WILLIAM W. BUCKINGHAM, and POUL OTTOSEN. *J. Thorac. Surg.*, 1951, 21: 34.

The authors review 93 consecutive pulmonary resections performed for pulmonary tuberculosis at the Missouri State Sanatorium, Mount Vernon, Missouri, from 1940 to 1949. Seventy-three of the patients were females and 20 were males. In the majority of patients there was more than one reason for resection, but clinical tuberculous bronchiectasis was the outstanding clinical finding. Epidural anesthesia was employed and it is believed that this greatly prevented the incidence of postoperative spreads and reactivations. In the present series, 91.9 per cent of living patients who underwent pulmonary resection are now sputum-negative for acid-fast bacilli.

STEPHEN A. ZIEMAN, M.D.

Report of a Series of Single Stage Thoracoplasties. R. C. LAIRD and C. E. LINDENFIELD. *J. Thorac. Surg.*, 1950, 20: 835.

The authors believe that single stage thoracoplasty is the operation of choice for many patients. The problem was approached cautiously at first because a single stage procedure was considered hazardous. The early cases consisted of patients in whom artificial pneumothorax was impossible to establish.

The results were encouraging beyond expectation. As experience increased, paradoxical movement of the chest wall failed to appear clinically to any significant degree, and postoperative shock was less than that seen in the second stage of a standard thoracoplasty.

Endotracheal cyclopropane anesthesia supplemented by small amounts of ether was used, and the incision parallels the medial border of the scapula, extending from the base of the neck to the anterior axillary line. The muscles are sectioned and the serratus fibers severed from the second rib. The first rib is removed entirely up to, and often including, the costal cartilage. Depending on the extent of the disease, all or moderately large portions of the second and third ribs are resected. Portions of the remaining ribs (fourth, fifth, sixth or seventh) are removed in such a way as to provide gradual tapering of the thoracic cage. The transverse processes of all ribs involved are resected routinely except that of the first. The incision is closed in layers with the scapula outside the ribs when the number removed is not more than five. When the sixth rib is taken out, the position of the scapula is ignored and it often falls of its own accord behind the ribs.

The operation was performed on 72 patients, with a minimum follow-up period of 16 months. The ages of these patients range from 15 years to 65 years. An additional 21 patients were subjected to the single stage procedure, 12 of whom had the sixth, and 2, the seventh rib operations. The results were very satisfactory.

It was concluded that complete thoracoplasty in one stage is a safe procedure in properly selected cases and that the one-stage thoracoplasty often permits adequate collapse to be obtained by the removal of fewer ribs than would be necessary in multiple-stage operations.

STEPHEN A. ZIEMAN, M.D.

Results of Surgical Treatment of Dilatations of the Bronchi (Résultats du traitement chirurgical des dilatations des bronches). J. MATHEY. *J. fr. méd. chir. thorac.*, 1950, 4: 433.

The author presents the results obtained in a series of 64 pulmonary resections performed on patients with bronchiectasis, during the period from 1945 to 1949.

Although there were only 2 postoperative deaths, complications developed in many of the patients after the operation; only 25 patients appeared to be free of all complications. The most frequent postoperative findings were atelectasis of the remaining lobe (21 cases) and bronchial fistula (9 cases). Atelectases occurred much more frequently in patients in whom only a part of the lobe was removed than in those having whole lobectomies. Bronchial fistulas occurred only in cases which were complicated by tuberculosis.

The late results were excellent in most cases. In 49 of the 64 patients, follow-up examination was possible; 35 of these were completely cured, 6 were improved considerably, whereas, in 8 patients the results were poor, partly because new bronchiectases had formed after the operation, partly because not all ectatic bronchi had been removed, and partly because of complicating tuberculosis.

WERNER M. SOLMITZ, M.D.

Transparietal Needle Biopsy of Tumors of the Lung (La ponction-biopsie transpariétale des tumeurs du poumon par la technique de Condorelli). A. CIONI. *J. fr. méd. chir. thorac.*, 1950, 4: 417.

Since 1928, needle biopsy has been utilized by the author in those instances in which a definitive diagnosis was not obtained by bronchoscopy or by other methods. The technique is most useful in those tumors which arise in the small distal bronchi beyond the reach of the bronchoscope.

The method is limited by the location of the lesion. Tumors located at a depth of more than 2 or 3 cm. in the pulmonary parenchyma (from the parietal pleura) should not have an attempted needle biopsy.

One danger is that of air embolism encountered by the needle entering the pulmonary vasculature; however, with the use of Condorelli's technique much of this danger is eliminated. The syringe is filled with serum to insure that no air is present, and after careful roentgen localization the tumor is aspirated while the operator aspirates constantly on the syringe as the needle is being inserted. The patient is instructed not to breathe after full expiration in order to prevent pleural or parenchymal damage.

Photomicrographs are presented which demonstrate quite clearly the certainty of diagnosis demonstrated by such methods. It is apparent that the author has had excellent results in obtaining pathologic diagnoses in lung tumors lying quite deep within the pulmonary parenchyma.

ORVILLE F. GRIMES, M.D.

Early Diagnosis of Carcinoma of the Lung. J. K. KRAAN. *Arch. chir. Neerl.*, 1950, 2: 201.

The author believes that carcinoma of the lung is now the easiest of any neoplasm to diagnose. Emphasis is placed on the irritating cough episode which is usually characterized as a dry cough. The merest streak of blood in the sputum should never be disregarded and when chest findings reveal a wheeze with slight dyspnea, and symptoms of so-called bronchitis appear, the condition becomes more serious. The patient should then be examined more thoroughly. The outcome of the laboratory analysis will depend almost entirely upon the locus, the

spread of the cancer, and the nature of the cells found. These latter may be one of three types: planocellular carcinoma, adenocarcinoma, or undifferentiated carcinomas.

The patient definitely should have bronchoscopy, which is considered a most valuable diagnostic aid. From bronchoscopy and cell studies it is possible to diagnose the great majority of lung carcinomas.

In the differential diagnosis, the following conditions should be considered: bronchial adenoma, tuberculosis, primary chronic abscess, atypical pneumonias, mediastinal cysts, neuronomas and lymphosarcomas, tuberculous lymph glands, malignant granuloma, intrathoracic struma, and fungoid infections of the lungs. STEPHEN A. ZIEMAN, M.D.

HEART AND PERICARDIUM

Surgical Relief of Congenital Cyanotic Heart Disease; Late Results in 72 Cases. T. HOLMES SELLORS and J. R. BELCHER. *Lancet*, Lond., 1950, 259: 887.

Seventy-two cases in which surgery was undertaken for the relief of congenital cyanosis are described. The minimal follow-up period was 6 months. Thirty of these patients were males and 42 were females. Forty-nine patients were between 5 and 15 years of age. Surgery was undertaken for:

	No. cases
Typical Fallot's tetralogy	65
Situs inversus and Fallot's tetralogy	2
Transposition of great vessels	2
Tricuspid atresia	1
Pulmonary stenosis only	2
	72

Associated abnormalities were:

	No. cases
Gross venous anomalies	8
Right-sided aortic arch	18
Chest wall deformity	19
Absent right pulmonary artery	1

Signs and symptoms of these anomalies were:

1. Cyanosis had been present since birth in 77 per cent of cases.

2. Dyspnea was classified into 4 groups, based on walking without resting: (a) less than 50 yards, 21 cases; (b) less than 200 yards, 29 cases; (c) less than a mile, 11 cases; and (d) more than a mile, 11 cases.

3. About 70 per cent assumed squatting positions to relieve the dyspnea of exertion.

4. Symptoms of irritability of the central nervous system may be attributed partly to chronic anoxia. An almost pathognomonic coyness or shyness disappeared after surgery.

5. Clubbing of the fingers which regressed in the year following surgery was present in all but 3 cases. These 3 patients had arachnodactyly.

6. A large number of patients had deformities of the chest, such as funnel chest and pigeon breast.

7. Polycythemia was usually present. The highest number of red blood cells was 10,000,000/mm³. Hemoglobin averaged between 130 and 170 per cent, the highest being 200 per cent. Oxygen saturation of the arterial blood varied between 66 and 71 per cent.

In most cases, it was found that the diagnosis could be made by x-ray and physical examinations. Cardioangiography should be reserved for conditions which are difficult to diagnose.

In 62 cases a left posterolateral incision was made and the left subclavian artery was anastomosed into the left pulmonary artery; the procedure was reversed in 2 cases of situs inversus. The technique employed is described in detail.

Among the first 25 cases, 6 deaths occurred. In 68 subsequent procedures (not all in this series), only 3 deaths occurred. This is attributed to the greater skill and experience gained in the early cases. Of the 9 deaths, 2 occurred as a result of cardiac irregularities, 4 others resulted probably from cardiac failure, and the remainder were caused by thrombosis or hemorrhage.

In the absence of complications, the postoperative course allowed discharge from the hospital in 2 weeks. Following discharge, improvement which started in the immediate postoperative period continued for as long as 9 months, as measured by exercise tolerance. One patient died 1 year after surgery, 7 patients showed no improvement following surgery, 42 were markedly benefited, and 22 were considerably improved. ROBERT L. CRAIG, M.D.

Clinical Diagnosis of Tumors of the Heart (Le diagnostic clinique des tumeurs du coeur). M. SEGERS and E. DELATTE. *Bruxelles méd.*, 1951, 31: 19.

The symptomatology of neoplasms of the heart is so variable that the diagnosis is usually made only at postmortem examination.

Primary tumors are less frequent than secondary tumors and may be benign or malignant. Among the latter, sarcoma predominates, while the most frequent benign tumor is myxoma; however, fibroma, lipoma, angioma, or rhabdomyoma may also be found. Secondary tumors extend usually by contiguity from neoplasms in the lungs, the esophagus, the pericardium, or the mediastinum. Less frequently dissemination in the heart is due to metastatic thrombi carried by the blood or the lymph stream.

Myxoma usually assumes the shape of a pedunculated polyp and is found most frequently in the left auricle. Transitory auscultatory manifestations of a mitral stenosis in an aged individual should focus the attention of the physician on this diagnosis, which may be corroborated by histologic examination of peripheral emboli of the tumor. Contrary to the Adams-Stokes' syndrome or the carotid sinus syndrome, syncope caused by occlusion of the mitral orifice by a myxomatous polyp is preceded by an attack of suffocation.

Neoplasms of the heart frequently produce pericarditis. In such cases aspiration may help to estab-

lish the correct diagnosis. Electrocardiographic changes, especially those affecting the ST segment, may simulate the image of a recent infarction, but they occur without clinical symptoms, last a long time, and are not accompanied by a depressed T wave or by systolic expansion visible in the course of fluoroscopic examination. The diagnosis may be confirmed by atypical roentgenographic deformities or by the presence of distant metastases.

While the diagnosis of secondary tumors of the heart is of purely academic interest, recognition of primary tumors is of clinical importance since the advance of surgery of the heart.

The authors succeeded in recognizing clinically a secondary tumor involving the right auricle and the anterior ventricular wall. The postmortem findings confirmed the diagnosis. JOSEPH K. NARAT, M.D.

Anastomosis of the Aorta by Direct Suture and by Homoimplants. Technique; Immediate and Remote Results; Anatomic Studies (Suturas y homoinjertos de aorta. Técnica, resultados inmediatos y alejados. Estudio anatómico.) ALFREDO LANARI and OSCAR CROXATTO. *An. Cáted. pat. clín. tuberc.*, B. Air., 1949, 11: 70.

The experimental animals were dogs weighing more than 12 kgm. In direct sutures, about 1 cm. of the aorta was excised and then anastomosed directly. Three of the dogs lived for periods of 4, 12, and 15 months, respectively. At the end of these periods—especially in the dog which lived 15 months—there was noted evidence of aneurysm formation at the points of suture; this was ascribed to the pull of the elastic walls of the aorta on the stitches during the process of healing. In these instances a temporary glass tube was inserted into the arterial stumps and the circulation of the blood through this glass tube was re-established by releasing the arterial clamps while the anastomosis by the mattress suture technique was completed for three-fourths of the circumference of the artery; then the artery clamps were temporarily reapplied, while the glass tube was extracted and the anastomosis completed. By this means the authors have been able to reduce the time of stoppage of the blood stream through the aorta to a period of less than the 15 minutes which they have accepted as the longest safe period for subjecting the more important organs and nerve centers of the body to interruption of the blood supply. Special emphasis is placed on the employment of penicillin during and after the operation.

The homoimplants used were fresh and all of about 6 cm. in length. The proximal anastomosis was done under blood stoppage conditions; however, the glass tube technique was employed for the performance of the peripheral anastomosis, again with the intent of reducing the period of anemia of the portions of the body distal to the interruption. However, in future work the authors intend to dispense with the glass tube technique as with the perfection of their technique it will be unnecessary for an abridgment of the anemic period.

From the results obtained with the homoimplants it is concluded that the implant method is superior to direct anastomosis. Seven of the animals operated upon in this manner by the authors lived for considerable periods after the operation. In these dogs the graft healed in perfectly. When these animals were eventually sacrificed and the grafts examined, it was found that all that remained of the line of suture was at most a shallow groove in the otherwise smooth walls. As a whole it was difficult to distinguish the grafted section from the normal aortic walls on each side. The most notable defect was the formation of masses of cartilage at the points of pressure of the arterial clamps. This phenomenon is ascribed to the transformation of the connective tissues of the intima at these points into a cartilaginous tissue which would require a less copious supply of nutrient blood; the authors do not think the process represents a true chondrogenesis eventuating in the formation of osseous tissues.

Microscopically, the elastic tissues of the walls of the recipient aorta and of the graft did not proliferate; the consolidation of the suture line seemed to have been accomplished by a proliferation of the connective tissues of the ends of the graft and of the recipient artery. This connective tissue proliferation united the ends of the arteries and reformed the intima and intimal endothelium. The intimal layer of the graft, it is true, thickened; however, this is taken by the authors to mean that the graft itself continued to live after the implantation and was passing through the process of sclerotic edema as described by Heuper (*Arch. Surg.*, 1944, 38: 245).

Another sign that was taken to indicate the continued postimplantation vitality of the graft was the finding of small areas of necrosis in the tissue of the intima. These processes may be explained under the hypothesis of accumulation of waste products in the deeper layers of the wall of the implant because of the relative isolation from the blood stream within the aorta. JOHN W. BRENNAN, M.D.

Aortic Resection and Anastomosis in Pups Studied after Reaching Adulthood. JAMES W. BROOKS. *Ann. Surg.*, 1950, 132: 1035.

The author conducted a series of experiments in which the aortas of young pups were resected and immediately anastomosed. A continuous, everting mattress suture of 5-0 silk was used, which penetrated all layers of the aortic wall. Subsequent studies, during life and after sacrifice, indicate that the area of anastomosis will increase in size with the growth of the animal, but not as much as the normal portion of the aorta. The degree of constriction varied from 17 to 50 per cent at the site of the anastomosis; the constriction was not sufficient to stimulate the development of collateral channels or to cause cardiac enlargement. Healing at the point of anastomosis was excellent and adequate to withstand normal aortic pressures.

ORVILLE F. GRIMES, M.D.

ESOPHAGUS AND MEDIASTINUM

Esophagoscopy in the Diagnosis and Treatment of Esophageal Disease. STANTON A. FRIEDBERG. *Surg. Clin. N. America*, 1951, 31: 3.

The author presents a detailed article on esophagoscopy, and the diagnosis and treatment of esophageal disease. Symptoms of esophageal disease, surgical anatomy, technique of anesthesia, and complications are among the things discussed.

Under the heading of diseases of the esophagus the author discusses both diagnosis and treatment. Congenital stenosis and congenital shortening are discussed under anomalies. Rupture of the esophagus, acute esophagitis, and corrosive injuries are considered under injuries and inflammations. Foreign bodies usually produce some degree of swallowing difficulty and, if sharp, cause pain. The technique of removal is briefly discussed. Under chronic diseases are discussed: (1) cicatricial stenosis of the esophagus, chronic hypopharyngitis, tuberculosis, syphilis, diverticula, hiatal hernia, varices, and neoplasms. The neurologic disturbances, which are discussed briefly, include functional dysphagia, bulbar nuclear involvement, and cardiospasm or achalasia.

W. FOSTER MONTGOMERY, M.D.

Roentgenologic Examination of the Esophagus. LILIAN DONALDSON. *Surg. Clin. N. America*, 1951, 31: 21.

The examination of the esophagus with spot films requires an x-ray machine which allows easy and rapid movement of the fluorescent screen during fluoroscopy and which can be instantly locked rigidly and switched to filming with a minimum of time and effort. Consistently poor quality of spot films may be ascribed mainly to four factors: (a) failure of the spot filming device to lock rigidly so that vibration blurs the film detail, (b) insufficiently fine focal spot for the relatively short focal spot-film distance inherent in the use of under-table tubes, (c) insufficiently fine stationary grid to clean up adequately the scattered secondary radiation from adjacent soft tissues, and (d) improper exposure factors.

The appearance of the normal condition, and the use of the Valsalva test in the examination of the hypopharynx and cervical esophagus are discussed. The use of the lateral projection to show Zenkers' diverticulum and the "web formation" in the Plummer-Vinson syndrome is stressed.

The technique of the examination of the intrathoracic esophagus is described. Scleroderma with shortening of the esophagus, neoplasms, varices, benign tumors, and diverticula are discussed.

W. FOSTER MONTGOMERY, M.D.

Congenital Deformities of the Esophagus. WILLIS J. POTTS. *Surg. Clin. N. America*, 1951, 31: 97.

Congenital deformities of the esophagus are rare but should be considered, in infants especially, as possible causes of dyspnea, dysphagia, abnormal vomiting or regurgitation, and unexplained attacks of cyanosis. These deformities are on an evolutionary or developmental basis. The pharynx, esophagus, stomach, larynx, trachea, lungs, and bronchi arise from the foregut, and up to the third week of embryonic life the esophagus and trachea are a single structure. During the third or fourth week a groove appears in the floor of the primitive foregut. It deepens and the margins fuse to form a septum between the esophagus and the trachea. Separation of the trachea and esophagus takes place last at the bifurcation of the trachea, and congenital deformities occur at that point. Complete absence of the esophagus is a very rare anomaly seen only in the monster fetus.

The most common anomaly of the esophagus is congenital atresia with tracheoesophageal fistula. The upper end of the esophagus may be connected with the trachea and the lower end be blind, both ends of the esophagus may be connected with the trachea, or the upper end of the esophagus may be blind and the lower end connected with the trachea. The anomaly is estimated to occur about once in 2,500 births. Excessive mucus and fluid are found in the throat immediately after delivery. Cyanotic attacks usually occur during the first 2 days of life. These findings plus regurgitation of unchanged food or fluid immediately after swallowing are diagnostic of congenital obstruction. Confirmation is made by passing a catheter as far as possible into the esophagus, injecting 2 c.c. of lipiodol, and taking a roentgenogram. Pneumonia, atelectasis, or both are complications, and the diagnosis should be made as early as possible. A blind end and no air in the gastrointestinal tract is indicative of atresia of the esophagus without tracheoesophageal fistula. Air in the stomach plus a blind upper end of the esophagus indicates atresia with tracheoesophageal fistula. Preoperative care includes the use of the oxygen tent and frequent throat aspiration. Nothing is given by mouth; sufficient fluid to supply the physical requirements is given but from 40 to 50 c.c. of fluid per pound of body weight, instead of the usual 60 to 75 c.c., are given. Not more than 10 c.c. of physiologic saline solution per pound of body weight should be given because of the danger of pulmonary edema. Antibiotic therapy is promptly begun. The position of the infant is changed frequently, and if atelectasis has occurred the child is laid on the opposite side. Usually a day is required to improve the child's condition. For anesthesia, ether given with the open mask has been found most satisfactory, although one should be prepared for emergency intratracheal intubation. Through a right parascapular incision, after resection of the third or fourth rib, an extrapleural identification of the lower esophageal segment is made and this is dissected out as far as seems necessary, transfixed, and cut near its attachment to the trachea. The upper end and larger end is dissected free as far as possible and a small opening is made to correspond with the lower opening. Anastomosis is then carried out, and the extrapleural space is

drained with a catheter which is left for about 10 days. Postoperative care consists of supplying the fluid requirements and continuing the antibiotics. Water by mouth is begun cautiously on the third day. Gastrostomy is avoided postoperatively, if possible. If healing is smooth, there is little danger of esophageal stricture. Of 27 patients in whom the operation was performed, 12 survived the operation and 11 are well and alive at present. The high mortality is due largely to the poor condition of the infant.

Congenital atresia of the esophagus without fistula with both ends of the esophagus ending in a blind pouch occurred in 3 of 37 cases seen at the Children's Memorial Hospital, Chicago. In none of these cases was it possible to anastomose the ends of the esophagus. Gastrostomy plus exteriorization of the upper end of the esophagus at the left side of the neck is life-saving, but does not solve the problem of re-establishing normal deglutition in this anomaly. Many procedures have been described, but the author believes that in the cases in which the ends of the esophagus cannot be brought together, a gastrostomy and exteriorization of the cervical end must be performed, and at a later age an esophagus is constructed in stages from the jejunum placed intrathoracically; then its upper end is anastomosed to the cervical portion of the esophagus and its distal end to the stomach.

Congenital stenosis of the esophagus usually does not become manifest until the infant begins to take solid foods. The point of stenosis is usually in the midportion of the esophagus. Near the diaphragm it may be mistaken for cardiospasm. Stenosis is easily demonstrated with x-rays, and relatively easily corrected by esophageal dilatation. Surgery is rarely indicated, but the author presents a case in which it was used because of the impossibility of even getting a thread through the stricture.

The congenitally short esophagus may not be recognized until adulthood when symptoms of ulcer prompt roentgen examination of the esophagus and stomach. It is often discovered in infancy after the swallowing of a foreign body. The diagnosis is made by means of fluoroscopy following oral administration of barium. A portion of the stomach appears above the diaphragm, and at the point where the esophagus enters the intrathoracic stomach there will usually be a stricture. The treatment in infants or children is esophageal dilatation, and a liquid diet may be necessary. Adults are advised to masticate food thoroughly. Ulcer symptoms of pain with bleeding are treated with frequent feeding and antacids.

Webbing of the esophagus is a rare anomaly which causes symptoms similar to those of congenital stricture of the esophagus. X-ray examination reveals small transverse defects in the column of barium. The treatment is dilatation.

Duplications of the esophagus are rounded, oval, or oblong; they are cystic and vary in size. Some are attached intimately to the esophagus and lie in the posterior mediastinum. Those entirely free from the esophagus may be found anywhere, but are usually in the central sector of the chest. The symptoms, which usually occur during the first 2 years of life, are dysphagia, respiratory embarrassment, cough, regurgitation, and occasionally hemoptysis. Cysts lined with gastric mucosa may perforate and produce signs of pulmonary infection. Roentgenograms show a smooth-walled mass of homogeneous density. Absolute diagnosis is made by thoracotomy. If the duplication is extensively attached to the esophagus it should be marsupialized to the chest wall. Eventually the mucous membrane of the duplication thus marsupialized must be removed surgically or by curettage because fistulas may otherwise result and persist.

Cardioesophageal relaxation or chalasia is usually associated with vomiting beginning during the first few days of life. This is a rather effortless vomiting, and the vomitus is usually not bile-stained. The infant is more likely to vomit when laid horizontally immediately after feeding. Chalasia is diagnosed roentgenographically by decreased peristalsis in the esophagus and apparent lack of tone in the organ. Barium is seen to regurgitate from the stomach into the esophagus on slight pressure or crying. Treatment is directed toward feeding in the erect position and keeping the baby in that position for at least a half an hour afterward. The condition corrects itself spontaneously in the course of a few weeks if the child's nutrition is maintained.

Cardiospasm or achalasia in infants produces symptoms of frequent vomiting and regurgitation; sometimes it does not occur until solid foods are added to the diet. In older children regurgitation, vomiting, and choking may appear suddenly in a hitherto normal child and periods of stress seem to aggravate the condition. Diagnosis is made by fluoroscopy which reveals a funnel-like dilatation of the esophagus tapering to a point at the cardia. The cause of the condition is not understood, but the treatment is esophageal dilatation; an occasional cure follows one dilatation. Surgical intervention is rarely indicated.

Obstruction of the esophagus by the external pressure of a congenital vascular ring may be caused by a number of vascular anomalies. The most common pressure defect in the esophagus is caused by the right subclavian vessel. A congenital abnormal development of the aorta, with a persistent anterior and posterior segment, results in a vascular ring surrounding the trachea and esophagus and may cause dysphagia, dyspnea, wheezing respirations, frequent upper respiratory infections, and attacks of cyanosis. If the arch of the aorta curves to the right and a persistent ductus arteriosus extends from the aorta behind the esophagus and curves forward to its communication with the pulmonary artery, similar symptoms may occur. Diagnosis is made after barium is given orally. If the symptoms warrant, the vascular anomaly must be corrected surgically.

JACOB T. BRADSHER, JR., M.D.

Peptic Disease of the Esophagus in the Adult
(Maladie peptique de l'oesophage chez l'adulte).
C. COUINAUD. *J. chir.*, Par., 1950, 66: 866.

Although peptic ulcer of the esophagus is rare, about 500 cases could be found in the literature.

This article is a comprehensive treatise covering the pathology, symptomatology, differential diagnosis, and treatment of the disease. The author differentiates two anatomic forms:

One is the peptic ulcer which resembles the peptic ulcer of the stomach and duodenum in all respects. It may be single or multiple, is situated at the lower end of the esophagus, mostly at the posterior wall, and extends into the muscularis. The ulcers often heal spontaneously, leaving a star-shaped whitish scar.

The other form is peptic esophagitis of the inferior third of the organ. No ulcers are present in this portion, but the entire mucosa is absent, and the lesions often involve the muscularis. Esophagitis is always accompanied by hyperchlorhydria and the reflux of gastric juice. Often gastroduodenal ulcer, pyloric stenosis, or diaphragmatic hernia with a short esophagus is present.

Complications include perforation and stenosis. The perforations occur most frequently into the mediastinum, the pleural cavity, or into both, and in rare cases into the pericardium or even into a bronchus. The stenoses may be of the spastic or the organic type and correspond point by point to pyloric stenoses of peptic ulcer. They can be permanently cured by dilatation, but only if and when the underlying process has healed.

The symptomatology includes pain, dysphagia, and regurgitation. Two types of pain are differentiated: pain at the time of deglutition, which is aggravated when spices, alcohol, or iced drinks are ingested, and the specific "peptic" pain which sets in 15 or 30 minutes after deglutition and corresponds to the pains experienced in peptic ulcer of the stomach and duodenum.

Roentgenographic examination may reveal stenosis of the distal end of the esophagus or a typical niche if the ulcer is sufficiently deep. However, shallow ulcers and peptic esophagitis frequently cannot be seen in the roentgenograms. The technique is even more difficult than in duodenal ulcer and requires several pictures in different directions and positions.

Esophagoscopy is the most important method of arriving at a correct diagnosis. It provides much better information than roentgenography; it is, however, contraindicated in bleeding ulcers and ulcers in danger of perforation.

A number of different factors play a role in the etiology. In some cases the disease is directly associated with gastroduodenal ulcers. Ectopic islands of gastric mucosa in the wall of the esophagus may be subjected to the same influences as the mucosa of the stomach proper and give rise to the formation of ulcer.

Other etiologic factors include diaphragmatic hernia of the esophageal hiatus and short esophagus, either congenital or acquired. Furthermore, a new type of esophageal ulcer has been observed frequently during the last few years as a sequel of stomach surgery. Interventions which permit free reflux of the stomach juice into the esophagus carry the danger of peptic ulcer or esophagitis. Such operations consist especially of esophagogastric anastomoses or cardioplasties for megaesophagus, and resections of the lower part of the esophagus for the treatment of benign lesions.

The treatment is conservative in most uncomplicated cases. It includes bed rest, diet, atropine in high doses, bismuth, and kaolin. Some authors reported spectacular results from treatment of the ulcer with 10 per cent silver nitrate through the esophagoscope. Others recommend temporary gastrostomy or jejunostomy if the ulcer is not healed by medical treatment within 2 months.

Intensity and persistence of the ulcer in spite of medical treatment, and especially a tendency toward hemorrhage are the indications for surgery. Vagotomy alone or combined with gastrectomy, or resection of the stomach followed by esophagogastrostomy or esophagojejunostomy has been performed successfully by different men.

Stenoses can be cured in many cases by dilatation, provided that the underlying esophagitis or ulcer has healed. As long as the esophagitis persists, dilatation treatment will never be successful.

WERNER M. SOLMITZ, M.D.

Cancer of the Supra-Aortic Esophagus; An Anatomoclinical Study and Surgical Contribution.
J. H. RESANO and T. ROCK. *J. internat. chir. thorax.*, 1950, 2: 195.

The authors review the case histories of 75 patients with carcinoma of the esophagus located in the supra-aortic segment. Their studies seem to indicate that esophageal carcinoma in this segment has a prognosis which is far less favorable than that of carcinomas in other locations in the esophagus. The technical difficulties involved in the resection of the involved area and the reconstruction of the gastrointestinal tract in the cervical region are considerable.

It is important to realize from the study of these 75 cases that, even in those in which diagnostic procedures were performed at a relatively early stage in the development of the lesion after the onset of symptoms, radical resection was impossible in many instances.

The anatomy involved, with respect to the supra-aortic segment of the esophagus, frequently limits radical excision of the tissue. The close association of the trachea, major vascular trunks, and recurrent nerves, as well as the frequency with which the malignancy appears to adhere either directly or indirectly to associated vital structures, often compels the surgeon to refrain from performing many radical resec-

tions or it may be necessary to confine his operation to a merely palliative procedure.

ORVILLE F. GRIMES, M.D.

Radical Operation of Carcinoma in the Upper Part of the Esophagus by Esophagogastrostomia Cervicalis (Die Radikaloperation des hochsitzenden Oesophaguskarzinoms mit Oesophagogastrostomia cervicalis). A. M. FEHR. *Helvet. chir. acta*, 1950, 17: 376.

Surgical treatment of carcinoma in the upper third of the esophagus, i.e., above the aortic arch, is a technically difficult problem. Until recently, most surgeons rejected intrathoracic anastomosis and preferred to join the stumps by antethoracic plastic operations. This procedure, however, entails a number of interventions over a period of several months and is a great strain on the patient.

Recently, intrathoracic anastomosis was performed by several workers. Altogether 8 cases are on record. After resection of a large portion of, or the entire, esophagus the stomach was joined to the pharynx either anterior (4 cases) or posterior (3 cases) to the aortic arch. In 1 case the right side of the thorax was chosen as the road of approach. Three patients succumbed, and 5 survived the intervention.

The author describes in detail 2 cases of his own. One of the patients died on the third postoperative day from heart failure, while the other made an uneventful recovery and was discharged 3½ weeks after the operation.

The writer emphasizes that mobilization and transposition of the stomach into the thorax is possible without any danger to the blood supply if only the right gastric artery and the right gastroepiploic artery are kept intact. All other vessels at the great and small curvatures may be ligated without risk

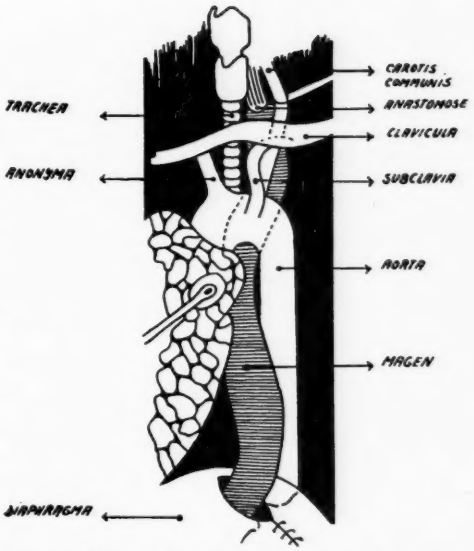

Fig. 1 (Fehr). Schematic drawing to show the transposition of the stomach posteriorly of the aorta with cervical esophagogastrostomy.

Fig. 2. Case 2, 3 weeks after operation. The cervical esophagogastrostomy is completely pervious. No congestion of the passage is caused by the aortic arch.

Fig. 3. Six weeks after operation. Undisturbed and fast emptying of the stomach. The pylorus lies close below the diaphragm.

of necrosis (method of Sweet). If the stomach is very small the duodenum can be mobilized also so that after the transposition the pylorus lies directly under the diaphragm.

The author believes that transposition of the stomach into the original bed of the esophagus, i.e., behind the hilus of the lung and the aortic arch, is preferable to the preaortic route for several reasons. The distance to the cervical area is shorter by 3 or 4 cm. and kinking of the stomach by the aortic arch is avoided. Furthermore, resection of the first rib and the clavicle is not necessary. Finally, the postoperative dilatation of the stomach which occurs regularly as a sequel of the vagotomy is kept within limits, and the compression of the lung and diminution of the respiratory surface is less significant than in the preaortic method.

The question is raised whether the postaortic method should not be used also in carcinoma of the middle third in cases in which the esophagus stump is too short to ensure a safe anastomosis in front of the aorta. WERNER M. SOLMITZ, M.D.

MISCELLANEOUS

Immediate Care of Thoracic Injuries. PAUL C. SAMSON. *Gen. Pract.*, Kansas City, 1951, 3: 39.

The author presents a scholarly approach to the basic problems incident to thoracic injuries. He outlines the fundamental concepts and pathological changes associated with intrathoracic injuries and presents them in a logical manner.

The use of intratracheal suction to combat excessive bronchial secretion or intrabronchial obstruction from inspissated mucus is emphasized. The life-saving value of such a simple procedure is of unquestionable aid in the care of extremely ill patients suffering with thoracic injuries. The author stresses this point with several well-outlined examples.

The remainder of the article outlines in succinct fashion the principles associated with the treatment of pneumothorax, hemothorax, emphysema, and complicated abdominal thoracic injuries.

ORVILLE F. GRIMES, M.D.

SURGERY OF THE ABDOMEN

ABDOMINAL WALL AND PERITONEUM

Ten Year Statistical Study of Inguinal Hernias. A Comparison of the Rate of Recurrence Following Repair by the Halsted I and Other Operations. JAMES J. CLEAR. *Arch. Surg.*, 1951, 62: 70.

The author presents a study based on the analysis of the case histories of 771 patients in whom 1,048 hernia repairs were performed. The majority of the hernias were repaired according to the Halsted I technique, i.e., by extra-aponeurotic transposition of the spermatic cord after high ligation of the sac. A minority were repaired by various other techniques.

In this recorded series there were 114 recurrences, a rate of 11 per cent. Seventy hernias, or 62 per cent, recurred within 5 years. Forty-four recurrences were found after 5 years, 38 per cent of the total number. Among the patients with bilateral hernias, there were 51 recurrences, or 9 per cent, which almost equaled the rate for unilateral hernias. Ten patients had bilateral recurrences. There were 53 cases in which recurrent hernias were repaired; these were followed up for 10 years and 21 recurrences, or 39 per cent, were found.

The pattern of recurrence time did not remain constant for different hernias repaired by various techniques. This study demonstrated that primary hernias repaired with surgical catgut according to Halsted I principles showed a peak recurrence at 1 year, whereas those repaired with silk showed a recurrence with three peaks: at 2, 6, and 10 years.

The use of nonabsorbable suture material was shown to be advantageous. There was a recurrence of 20.3 per cent when surgical catgut was utilized for primary hernias, but when silk suture material was used the recurrence rate was only 15.5 per cent. Fifty per cent of the recurrent hernias repaired with surgical catgut recurred, whereas there was a recurrence rate of 33.3 per cent when silk was used. When fascia was utilized as suture material on recurrent hernias, the recurrence rate was 45 per cent.

ORVILLE F. GRIMES, M.D.

Cysts of the Mesentery (Quistes del mesenterio). LEOCADIO SERRADA DIAZ and ANTONIO SERRADA DEL RIO. *Rev. espan. enferm. ap. digest.*, 1950, 9: 641.

A 58 year old man was seized by intense epigastric pain while working in the fields 1 month before he presented himself for treatment. The pain lasted all night, while he was working as a river fisherman, but it left him after sleeping. Following the noon meal of the next day the pain returned, this time in the region of the stomach but radiating to the genital organs. The patient had the sensation of something in his abdomen falling downward with erect posture. Fifteen days later the pain recurred and he was referred to surgery.

The abdomen was enlarged and rounded and palpation disclosed a huge tumor. This mass was of firm consistency, of irregular border, and slightly movable in its upper region but fixed in the lower. It gave the impression of being implanted in the right iliac fossa. Percussion revealed dullness over most of the abdomen which continued with that of the liver; tympany was elicited only in the left hypochondrium and in the left iliac fossa.

The blood examination at this time suggested an infective process; however, the patient remained in the hospital for 20 days and at the end of this period the blood picture was normal. Three attempts to fill the colon with a barium enema beyond the middle of the transverse colon failed; however, a later roentgenogram disclosed a fairly normal colonic roentgenographic picture with the sole exception that this organ appeared to be pushed peripherally by the large central mass of the tumor.

At operation the abdomen was found to be filled with a huge cystic mass developing between the serous layers of the mesentery of the jejunum for about 60 cm. of its length. The cyst was implanted in greater part deep to its root; the mesentery was, of course, thickened and highly vascularized. The cyst itself had formed adhesions with the parietal peritoneum, with the bladder, and particularly with the peritoneum of the right iliac fossa. The mass, nevertheless, was successfully removed and the wound closed without drainage.

The cyst, even after the withdrawal of 500 c.c. of content during the operation, measured 21 by 22 cm. When opened the cystic sac gave issue to a large amount of chocolate-colored fluid. There remained a considerable quantity of fibrinous, spongy material, of the same color as the extracted fluid. In the upper part of the cavity there was a fist-sized pocket containing a thick whitish-yellow liquid of purulent appearance, the pocket was thickened and there was a part of the wall the size of the hand which was apparently devitalized and necrotic. This last finding probably accounts for the septic blood picture of the patient upon admittance. Nevertheless, healing was practically without event and the patient was discharged as cured on the eleventh day. A month later the patient was in excellent health.

The histologic findings were those of the usual mesenteric cyst; there was no evidence of malignancy. There was no epithelial lining to the cavity, which raised the question as to whether the lesion originally started as a hemorrhage; however, there was no history of trauma to the region and the authors would prefer to consider the original etiologic agent to be an ordinary chylous or serous cyst which later gave rise to bleeding within the cyst cavity itself.

The authors believe that the treatment of these cysts should always be surgical and, preferably, total

excision, with marsupialization reserved for the rare instances in which total excision would seem contraindicated. Of course, the blood supply to the involved intestine must be respected and in cases in which the intestine would have to be resected with the tumor the prognosis would be more or less affected; however, this resection would, in the authors' opinion, be preferable to marsupialization.

JOHN W. BRENNAN, M.D.

GASTROINTESTINAL TRACT

Blood Vessels of a Gastric Ulcer. JAMES A. KEY. *Brit. M. J.*, 1950, 2: 1464.

Specimens of gastric ulcer removed at operation were examined by microangiography. A detailed description of the technique is included.

In a chronic ulcer, widespread vascular occlusion in the base of the ulcer, and extending along the line of the lesser curvature deep to the mucosa, can be demonstrated. In an acute ulcer there is an acute vascular disturbance occurring immediately beneath the mucous membrane—a hypervascularity, not an ischemia. These findings lend support to the hypothesis that in peptic ulcer an acute vascular disturbance occurs in the submucosa, and that the breach of the mucosa itself results from this underlying vascular derangement.

Such an hypothesis is of interest when compared to the observations of Wolf and Wolff on their patient with a large gastric fistula. They noted that during acute emotion the exposed gastric mucosa became engorged and finally produced scattered acute erosions. CURTIS ARTZ, M.D.

Clinicostatistical Findings on 200 Perforations of Gastroduodenal Ulcers into the Free Peritoneal Cavity (Rilieve clinico-statistici su 200 perforazioni di ulcera gastro-duodenale in peritoneo libero). ANTONELLO FRANCHINI. *Arch. ital. mal. app. diger.*, 1950, 16: 329.

Two hundred cases of perforation of gastroduodenal ulcer were observed at the Surgical Clinic of the University of Bologna, Italy, in the period from October, 1938 to October, 1948. Eighty-two of the patients appeared during the war influx into Bologna in the 3 years from 1941 to 1944. The greatest number presented themselves in the fall season (31.0 per cent) and the lowest number in the winter (16.5 per cent). Males comprised 191 of these 200 patients, the author ascribing this preponderance in part to the greater incidence of gastrointestinal ulcers in the male. Four-fifths of the patients presented preliminary typical symptoms of ulcer from months to years preceding the attack, and in a full third, the symptoms antedated the attack by more than 5 years.

Most (38.6%) of the perforations occurred during the evening without, however, being ascribable to excessive eating or to trauma. The operative mortality seemed to be bound up almost exclusively with the time elapsing between the perforation and the operative interference; naturally the influence of advancing age exhibited a certain influence on the mortality.

In more than 90 per cent of the cases the perforation occurred on the anterior wall of the duodenum and averaged from 3 to 5 cm. in diameter.

At the author's clinic the type of operation is chosen on an eclectic basis. Palliative operation (suture) was done in 102 cases with a mortality of 17.6 per cent; the radical procedures (Polya-Reichel, Polya-Hoffmeister, radical cure of peptic ulcer) were resorted to in 98 cases with an operative mortality of 10.3 per cent. This apparent advantage of the radical procedures is, of course, largely due to the fact that the less favorable cases were selected for the less radical operation. The real disadvantage of the palliative methods is evident, however, in the late results. In 92 per cent of the radically operated cases the cure was complete and permanent. In the sutured cases, on the contrary, definitive cure was obtained in only 28 per cent. The remaining 72 per cent of the patients complained of more or less persistent and intense suffering, many from postoperative pyloric stenosis.

All results have improved remarkably since the introduction of the antibiotics.

JOHN W. BRENNAN, M.D.

Vagotomy as a Treatment for Marginal Ulcer. GEORGE CRILE, JR., and GEORGE M. BROWN, JR. *Gastroenterology*, 1951, 17: 14.

Thirty-nine patients with a diagnosis of marginal ulcer were treated by vagotomy at the Cleveland Clinic during the last 4 years. The results are known in 36 of the 39 patients whose cases had been followed for periods ranging from 6 to 44 months. There were no operative or hospital deaths in the group. All patients classified as having proved marginal ulcers showed a definite ulceration at the enterostomy stoma, which was confirmed either by direct visualization, palpation, or microscopic examination of excised specimens, a history of massive bleeding with hematemesis or tarry stools following the last definitive operation, and a history of perforation following the last definitive operation.

In only 3 patients were the results considered as a failure. It is concluded that the results of vagotomy in the treatment of marginal ulcer are at least comparable to those following extensive gastric resection; its safety commends it as a standard treatment of marginal ulcer occurring either after gastric resection or gastroenterostomy.

STEPHEN A. ZIEMAN, M.D.

An Evaluation of Subtotal Gastrectomy for Gastric and Duodenal Lesions; A Postoperative Survey of 100 Cases. LAWRENCE SINGMASTER and GILSON COLBY ENGEL. *Gastroenterology*, 1951, 17: 1.

The authors present the results obtained in 100 living patients who had undergone gastrectomy. There were 78 male patients, of whom, 5 were negroes and 22 were white females. Fourteen patients

had malignant lesions of the stomach as confirmed at operation. In the remaining 86 patients the lesions were benign and consisted of 49 duodenal ulcers, 32 gastric ulcers, 3 marginal ulcers following previous gastroenterostomies, 1 gastric and duodenal ulcer, and 1 neurinoma of the stomach with hemorrhage.

The Polya antecolic type of anastomosis is recommended in the surgical treatment of these lesions and it is believed that this factor alone accounts for the absence of any "dumping syndrome" being observed in the group.

Three-hour glucose tolerance tests, fluoroscopic studies, and gastric emptying times have been obtained for correlation with the symptoms and the physical status of each patient. As compared with the normal glucose tolerance curve, this series revealed an early hyperglycemia followed by a hypoglycemia which had not returned to the normal level within 3 hours. This divergence from the normal curve was not found to be a causative factor in producing postoperative symptoms. Fluoroscopy, moreover, disclosed that final gastric emptying times were definitely shorter in this series of stomachs than in unresected stomachs. Under fluoroscopic observation, no evidence of abnormal jejunal distention was seen in any case during the progress of barium into the jejunum.

It is concluded that subtotal gastric resection is the procedure of choice in dealing with all benign gastric ulcers, or with duodenal ulcers which are not amenable to medical treatment.

STEPHEN A. ZIEMAN, M.D.

The Late Results of Partial Gastrectomy. B. B. MILSTEIN. *Ann. Surg.*, 1951, 133: 1.

This is a study of 101 patients who underwent partial gastrectomy for peptic ulcer in the University College Hospital, London, England, in the period from January, 1940 to September, 1947. Of the 90 living patients, 76 are males and 14 females; 37 had had gastric ulcer, 40 duodenal ulcer, and 4 anastomotic ulcer. The remainder had had pyloric or combined ulcers. Operations were performed for intractibility, recurrence, repeated hematemesis, pyloric obstruction, or hourglass contracture. About three-fourths of the stomach was removed. The anastomoses were retrocolic, no-loop, anisoperistaltic, end-to-side, or partly end-to-side. In 8 cases pyloric exclusion was performed. Microscopic cancer was found in 3 cases. Many factors considered in gastrectomy are dependent upon the time interval since surgery. One example is the level of free hydrochloric acid. Investigation was done by interviews, insulin and histamine, test meals and physical examinations. Examination by means of x-rays and blood studies were done as indicated.

Of the 5 deaths, only 1 was related to the original condition. This was a case in which the base of the gastric ulcer was not excised from the pancreas and death occurred as the result of gastric carcinoma 5 years after surgery. Postoperatively, 53 of the patients could eat any kind of food, whereas 30 were unable to eat some foods. Fifty-three had a very good appetite, 26 a fairly good one, and 7 had a poor appetite. Eighty-one of 89 patients were entirely free from pain. Severe pain was present in 6; 2 of these had colicky pain. One had pain similar to that which had been relieved by alkalis before the operation. Sixty-eight patients were free of flatulence and 11 complained of severe distention. This was usually relieved by lying down. The early postprandial syndrome occurred in 19.3 per cent and the late syndrome in 18.2 per cent. The statistics suggest that the early syndrome is less likely to occur when the partly end-to-side technique is used, but that the late syndrome is unaffected by the anastomoses. The author questions the current view, which seems to be that achlorhydria must be achieved in order to cure the patient.

On the average, the patient was away from his work on account of the operation from 2 to 5 months. Some of this delay may be explained by the advice of the referring physician or the industrial medical officer. However, the patient's condition should be the deciding factor in his return to employment. Fifty-nine of 72 patients gained weight, usually to the preoperative level. The incidence of recurrent ulceration was 1 per cent.

ROBERT E. FLORER, M.D.

Observations on Blood Flow in the Human Intestine. JOHN GRAYSON. *Brit. M. J.*, 1950, 2: 1465.

The temperature of any animal tissue exposed to an environment at a temperature different from that of the blood depends in part on the blood flow through the organ, and can be used to detect blood flow change. This principle was used to detect blood flow changes in exposed colostomies. Several experiments were carried out on patients to relate the bowel blood flow changes, which occur during heating or cooling of the body, to blood pressure changes.

Cold stimulus applied to the body surface produced cutaneous vasoconstrictions, intestinal vasodilatation, and a temporary rise in blood pressure. Removal of this stimulus produced cutaneous vasodilatation, intestinal vasoconstriction, and a temporary fall in blood pressure. Procaine hydrochloride injected into the exposed bowel relaxed vasomotor tone and prevented the occurrence of vasoconstriction in response to heat, and of vasodilatation in response to cold, although the vasoconstrictor action of intravenous adrenalin was not affected. It is suggested that the intestinal effects are brought about reflexly through the alterations in blood pressure.

CURTIS ARTZ, M.D.

Intestinal Obstruction in Infants and Children. KENNETH C. SAWYER and HORACE P. MARVIN. *Arch. Surg.*, 1951, 62: 1.

The management of intestinal obstruction in infants and children is quite similar to that in adults, although the inability of children to withstand distention and acute fluid loss makes early recognition and immediate definitive treatment imperative.

The manifestations of intestinal obstruction in infants and children are usually definite, although the severity of symptoms varies considerably, depending upon the type and location of the obstruction. Pain is the earliest and most constant symptom, usually accompanied by some degree of abdominal distention.

Treatment must be considered as primarily operative and of an emergency nature. Operative management is much the same as that employed in adults although children do not tolerate an enterostomy or exterioration of the bowel for any length of time because of the difficulty in maintaining proper fluid balance. Division of adhesions, releasing the bowel from some type of compression, reduction of intussusception, enteroanastomosis around an obstruction and/or excision of obstructed segments are the principal procedures to be considered.

Decompression by gastrointestinal suction, blood transfusions, fluid replacement, use of oxygen, sedation, and chemotherapy, plus excellent nursing care, are invaluable adjuncts to the operative procedure. Intestinal intubation may relieve distention and permit some delay in operation in order to improve the patient's general condition. Oftentimes intubation may serve to locate the obstruction preoperatively; however, gastrointestinal suction may mask a strangulated obstruction because of the improvement of symptoms and signs after a period of decompression. It is always vital to maintain proper water and chemical balance in young patients.

The author presents brief case histories of patients who were treated for various types of intestinal obstruction. ORVILLE F. GRIMES, M.D.

Submucous Lipomas of the Small Intestine. FRANKLIN R. SMITH and CHARLES W. MAYO. *Am. J. Surg.*, 1950, 80: 922.

Symptomatic lipomas of the small bowel are unusual. The report of such cases serves to focus attention on the place of benign tumors in the differential diagnosis of intestinal obstruction (particularly by intussusception), unexplained melena, and epigastric distress.

The incidence of subclinical lipoma of the small intestine found in their study, and reported by the authors in the complete paper, was 1 per 325 autopsies.

Records of 67 cases of lipoma of the small bowel are available in the files of the Mayo Clinic, and were included in the study. In 53 of the cases the lipoma was subclinical and was discovered at autopsy, in 9 cases it was symptomatic and required definitive operation, and in 5 cases it was found during operation for other gastrointestinal lesions. It appears that surgically significant lipoma is nearly three times as common in the large intestine as in the small intestine, although that structure is but one-fifth the length of the small intestine. Intussusception was the event that generally led to the diagnosis of lipoma in the 9 cases in which the tumor caused symptoms. Pain, epigastric distress, palpable abdominal mass, emesis, and change in bowel habit were the most frequent symptoms. Bleeding from the rectum occurred in only about one-fourth of these 9 cases although two-thirds of the lesions showed ulceration of the mucosa covering them. The duration of symptoms averaged 3 years and 3 months, but ranged from 2 days to 6 years.

The average age of individuals with symptomatic tumors was 54 years and the range in age was from 37 to 69 years. Two-thirds of the symptomatic lipomas occurred in males. Most of the lesions were found by roentgenographic and roentgenoscopic examination.

When a diagnosis of lipoma has been made the lesion should be removed immediately, whether the patient has symptoms or not, because of the potential hazards of erosion and intussusception. Furthermore, the benignity of the lesion cannot be determined from the roentgenologic examination or history.

Considerations with Reference to a Case of Duodenitis Purulenta (Considerazioni sopra un caso di duodenite purulenta). M. A. DINA. *Arch. ital. mal. app. diger.*, 1950, 16: 247.

The present case of duodenitis purulenta represents the twenty-seventh observation of this condition that has been reported in the literature available to the author. Other terms used to designate this affection are purulent, or suppurative, or phlegmonous duodenitis, abscess of the duodenum, diffuse and circumscript phlegmon of the duodenum.

The patient was a 51 year old male, a butcher by trade, who suffered a week of indisposition about 3 months before his death. There were chills, sweating, and fever. Later the patient lost his appetite and the abdomen began to swell. In the interval, laboratory tests were positive for brucellosis; treatment with vaccine was instituted and later tests were consistently negative. However, the patient disclosed a slight icterus and was treated with hepatic extract, cholagogues, and lipotropic factors. The icterus became more pronounced, with discolored feces and intermittent biliary urine. Edema of the lower extremities and hemorrhagic manifestations developed, with fever (38.5°C.), vomiting attacks, and pains in the epigastrium radiating to the back, especially to the lumbar region; ascites appeared. There was no polymorphoneutrophilic reaction; the patient became comatose and died a few days after entering the hospital. (The last attack lasted for about 5 days.)

At autopsy the diagnosis was subacute yellow atrophy of the liver, beginning atrophic liver atrophy, icterus, ascites, esophageal varices, duodenitis purulenta, mild gastrointestinal catarrh, diffuse petechial, subserous (pleura, epicardium, peritoneum) hemorrhages, subacute toxi-infective and hyperplastic tumor of the spleen (700 gm.), pulmonary hypostasis with minute bronchopneumonic foci, and right-sided total, left-sided partial, fibroadhesive pleuritis.

The liver was reduced in size (1,200 gm.), particularly marked with reference to the right lobe. The cellular arrangement of the parenchyma was disturbed and the liver cells themselves showed evidence of degenerative changes; the entire liver lobule was infiltrated with polymorphonuclear neutrophile cells. The intrahepatic biliary passages were filled with light-colored turbid bile. The gall bladder exhibited thickened, edematous walls and contained a turbid, thickened bile of a dark brown color.

The duodenum presented the appearance of a thick, recurved tube with edema of the surrounding tissues. The walls of the duodenum were thickened (about 1 cm.), the mucosa was characterized by coarse plications and intervening sulci, resembling the cerebral configuration. There was no evidence anywhere of a solution of continuity. Beneath the mucosa the walls presented a thickened tumid consistency, and on squeezing emitted a grayish-yellowish-greenish, turbid fluid. The cut section showed hemorrhagic spots and reddish striae. These lesions became gradually less distal, towards the ligament of Treitz, and ceased abruptly at the level of the pyloric ring. The papilla of Vater protruded in the form of a nut-sized nodule and could be sounded only with difficulty. The choledochus contained a hyperchromic, turbid bile. The head of the pancreas was somewhat edematous and softened. The lymph glands about the pancreas and the hilus of the liver were markedly tumefied, softened, succulent, and reddened.

On microscopic examination the duodenum exhibited a mucosa of practically normal thickness, and was not markedly altered; there was present some leucocytic infiltration and some congestion, and the muscularis mucosae was well delineated and fairly well preserved. The mucosal stratum, however, was separated from the muscular coat of the duodenum by an enormous thickening of the submucous layer. The loose connective tissue of this layer was permeated by a plasmatic exudate, rich in fibrin, wherein was observable (in addition to the red blood cells and their detritus) numerous cellular elements, in some places densely crowded together, in other places sparse and relatively isolated. This cellular infiltration was composed predominantly of polymorphoneutrophilic leucocytes in various stages of conservation. Here the blood vessels were enormously dilated and presented mural lesions. There were leucocytic plugs in the blood vessels and in the lymph spaces. Staining for bacteria in these sections gave evidence of rare bacilli.

The findings in the spleen were those of the usual septic swelling. The pancreas was edematous and showed evidence of marked postmortem autolysis. The enlarged lymph glands gave evidence of intrasinal desquamation and the presence of a few polynuclear leucocytes.

The author believes that the primary factor in the etiology was a congestion and condition of achlorhydria, paralyzing the conductive functions of the duodenum and rendering it more of an absorptive organ. This abnormal absorption resulted in the ingress into the submucosa of proteins which had not been far enough broken down and which acted as an irritant (foreign body irritation), with consequent edematous succulence of the submucous tissue. This in turn formed a favorable nidus for the ingress of the infective agents, perhaps arriving through the blood stream. The author is unable to explain adequately why the mucosa was so little involved and why the condition itself is so rare in relation to the other forms of intestinal and gastric inflammatory processes. He also admits that he does not understand why, if the primary etiologic factor consists of inflammatory processes in the liver and gall bladder regions (which is so prevalent in women), the condition should be encountered more frequently in the male sex. JOHN W. BRENNAN, M.D.

Conservative Surgery of Duodenal Ulcer. EDWARD MACLELLAN. *Lancet*, Lond., 1951, 260: 257.

This is a review of an operation designed by Wilson Hey, and slightly modified by the author. The purpose of the operation is to reduce the blood supply of the stomach and to interrupt the nerve pathways to this organ at several points. Permanent ligatures are placed along both curvatures of the stomach in such a way that much of the blood supply is cut off and most of the branches of the vagus and sympathetic nerves are blocked. A small hole is made in the gastrohepatic omentum, through which two fingers are passed so that the vessels running along the lesser curvature may be grasped between fingers and thumb. The stomach is pulled down and the aneurysm needle threaded with stout nylon is passed close to the stomach. The ligature, which embraces the vessels, nerves, and some omentum, is tied off with a triple knot just tight enough to obliterate the vessels. The branches of the vagus are not specially sought, but most of them are

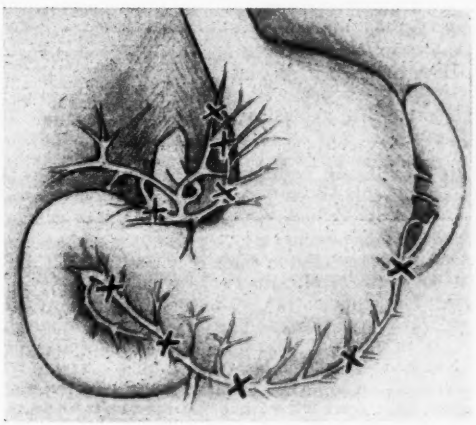

Fig. 1 (MacLellan). Approximate positions of ligatures.

automatically included in the ligatures. A hole is next made in the transverse mesocolon, and the main vessels along the greater curvature are tied in a similar way. The stomach now looks slightly cyanosed and somewhat contracted. A posterior gastroenterostomy completes the operation.

This operation has been done on a hundred patients in 10 years. There have been no deaths and only one anastomotic ulcer. Ninety-two patients consider themselves completely cured, are back at work, and gained an average of 16 pounds. Five patients still complain of pain at times. Three operations must be considered failures. Several patients had a temporary achlorhydria, but in one patient it persisted with troublesome diarrhea. This was completely controlled with hydrochloric acid.

The operation reduces the acidity in many cases, but not in all. In some cases the acid curve is still above normal, yet the symptoms have gone. It may be that interruption of the nervous pathways protects the stomach from the turmoil of a troubled mind, and many minds are troubled nowadays.

The author believes that modern civilization denies the stomach a chance to work on unprepared and uncooked foods and that the silver spoon aids and abets in its deterioration, so that degeneration and decay occur within the dark recesses of the stomach and duodenum. CHARLES BARON, M.D.

Routine Examination of the Lower Bowel; Results in 500 Asymptomatic Patients. VINCENT T. YOUNG. *Am. J. Surg.*, 1951, 81: 18.

The author has reported routine proctosigmoidoscopic findings on 500 adult patients who had no bowel complaints. Of this group 138, or 27.6 per cent, had some proctological lesion; 12.8 per cent had hemorrhoids which required treatment and 8.8 per cent had polyps. Diverticula, fissures, hypertrophic papillae, pruritus ani, and cancer of the lower bowel were other conditions found. The malignant tumors were operable and without extension.

It is obvious from this study that the diagnosis of precancerous lesions such as polyps and the diagnosis of carcinoma in a stage in which surgery can be effective in its treatment depend upon proctosigmoidoscopic examinations made before symptoms appear. THOMAS C. DOUGLASS, M.D.

Late Results of Vagotomy in the Treatment of Idiopathic Ulcerative Colitis and Regional Enteritis. FRANK D. EDDY. *Surgery*, 1951, 29: 11.

The author presents a follow-up study and analysis of data presented in three previous articles from the Department of Surgery, University of Minnesota. This study dates 3 years from the time the first case was vagotomized and includes complete clinical and laboratory data on the 39 patients now alive.

The need for such a close follow-up is adequately demonstrated by the fact that in patients with idiopathic colitis, who have had the disease 5 years or more, 15 per cent are predisposed to cancer of the colon, and another 15 per cent to cirrhosis of the liver.

Data covering the original 42 cases, the diagnosis, and the surgery done prior to vagotomy, are given by the author. Average times are given for the length of disease—58 months, with extremes of 5 weeks to 15 years, and the time between operation and the present study, 18.9 months. Age distribution in these cases was 6 to 71 years.

The condition of many of these patients on admission necessitated a regimen of intravenous feeding consisting of 10 to 20 per cent dextrose.

Six interesting cases are presented to illustrate the types of response and the different initial complaints.

Few of the patients showed dramatic return to normalcy, the usual course being a lapse into a quiescent state with healing of the involved bowel. The clinical improvement is broken down and a comparison is made of the extent and location of the original disease with follow-up result.

The author summarizes the surgery performed in this group of patients. Two patients underwent a second vagotomy and 1 patient had to be operated upon for gastric retention. The proctoscopic findings in the 29 cases available at the time are also given. The findings in 9 cases were normal, in 11 cases improvement with healing was shown, while in 6 cases active disease persisted.

There is a summary of the barium enema findings in these cases. Eight patients showed definite improvement, 7 no change, and 6, active progression and, finally, the time required for the passage of barium through the bowel, and the definite increase after vagotomy are shown.

In 29 cases the Hollander insulin test was used before and after operation. In 2 cases the preoperative test was negative and in 27, positive; in 26 of these the positive response was abolished by vagotomy. One case remained positive.

Following a review of the results, an attempt is made to set up criteria for future cases. Four factors were common in the overall picture: (1) gross bleeding to a marked degree; (2) fibrosis and scarring of the colon; (3) extensive ulceration as evidenced by proctoscopy or barium enema; (4) disease of 5 years or more.

The author discusses the possibly beneficial role played by vagotomy in these cases but arrives at no definite conclusions since the anatomical distribution and function of these nerves in the bowel is poorly understood. Vagotomy appears to benefit the patient by decreasing intestinal motility and spasm. It seems to interrupt a cycle of nervous and emotional imbalance affecting the colon and acts as if the distribution of the vagus nerves extended to the distal colon and rectum. CURTIS ARTZ, M.D.

One-Stage Resection of Entire Colon and Rectum for Ulcerative Colitis and Polypoid Adenomatosis. MARK M. RAVITCH and JACOB C. HANDELSMAN. *Bull. Johns Hopkins Hosp.*, 1951, 88: 59.

Resection of the entire colon, rectum, and anus is frequently indicated in two chronic nonmalignant

conditions: polypoid adenomatosis of the colon and chronic ulcerative colitis.

Ten patients, 4 with congenital polyposis of the colon and 6 with chronic ulcerative colitis, were subjected to one-stage abdominoperineal resection of the entire colon and rectum at Johns Hopkins Hospital, Baltimore. There were no deaths. A detailed, well illustrated description of the technique of operative procedure is given. The 10 case histories are briefly presented.

In 7 cases anal ileostomy was carried out. Temporary peroneal palsy in one patient and a pelvic hematoma in another were the only complications.

The technical feasibility of this operation and the successful convalescence of the patients indicate the applicability of this procedure when resection of the entire colon is required. CURTIS ARTZ, M.D.

Hemangioma of the Colon. W. WAYNE BABCOCK and KARL C. JONAS. *Am. J. Surg.*, 1950, 80: 854.

The authors report a case of hemangioma of the colon with treatment by a combined abdominoperineal sphincter-preserving operation, the first report in the literature of the disease with treatment by this technique.

The patient was a 17 year old male who had experienced rectal bleeding since birth. Two months before hospital admission he had an exsanguinating hemorrhage for which he received multiple transfusions.

The lesion extended from the ampulla of the rectum proximally to the point where the bowel crossed the pelvic brim. The submucosa and serosal layers were involved, the mucosal and muscular layers showing no significant change. Reddened and engorged mucosa was the only positive proctoscopic finding.

Thirteen months following operation the patient was in good health, complained of no recurrence of rectal bleeding, and had good bowel function and complete fecal continence.

Of the 3 other hemangiomas of the colon treated surgically which were reported in the literature, 2 were removed by Mikulicz resection and 1 was removed by the Lahey two-stage modification of the Miles combined abdominoperineal resection.

FREDERICK W. PRESTON, M.D.

Submucous Lipoma of the Large Bowel; Case Report with Review of the Literature. HAROLD N. CAVANAUGH. *Am. J. Surg.*, 1950, 80: 860.

The authors found 151 cases of submucous lipoma of the large bowel reported in the literature and added 1 case of their own.

The disease is frequently confused with carcinoma since it is generally seen in the cancer age group and produces similar roentgenographic findings. It is more common in women. In 21 cases reported since 1941 the symptoms in order of frequency were pain, constipation, diarrhea, melena, weight loss, nausea, gas, vomiting, and tenesmus. The locations of the tumors in order of frequency were the transverse colon, cecum, descending colon, sigmoid, ascending colon, and the two flexures.

These tumors occasionally become pedunculated and in 1 of 21 cases the tumor passed spontaneously.

The tumor in the author's patient measured 7 by 4 by 3 cm. It was treated by resection of the tumor and 10 cm. of the adjacent colon, followed by end-to-end anastomosis. Resection was the treatment employed in all but 3 of the cases reviewed; local excision was done in these 3 cases.

FREDERICK W. PRESTON, M.D.

An Evaluation of Oxygen Therapy as an Adjunct in the Postoperative Management of Carcinoma of the Rectum and Sigmoid Colon. LLOYD F. SHERMAN and HARRY E. BACON. *Am. J. Surg.*, 1951, 81: 105.

The authors have studied 5 groups of patients preoperatively and postoperatively. In this study it was found that the oxygen saturation in the arterial blood was depressed considerably by morphine given before the operation. The anoxia was much less when dilaudid was used. Spinal anesthesia apparently does not produce anoxia.

In 8 patients the use of Boothby oxygen masks raised the oxygen saturation dramatically in the postoperative period. This method was much more efficient than oxygen given by means of an intranasal catheter, following which the arterial saturation was somewhat lower. THOMAS C. DOUGLASS, M.D.

Surgical Aspect of Sigmoiditis (Aspects chirurgicaux des sigmoïdites). J. SÉNÈQUE and C. CREPY. *J. chir.*, Par., 1950, 66: 725.

The polymorphism of sigmoiditis explains the variability of its potential evolution.

Approximately one-third of the cases are undoubtedly of diverticular origin, a very small percentage are of primary character, and the rest are of doubtful origin. Various forms of sigmoiditis bear close clinical resemblance to pathologic lesions of the appendix, but no therapeutic implications can be drawn from this comparison.

Endoscopic examination should be supplemented by repeated roentgenographic studies. At least 3 films should be taken each time: the first during the introduction of the opaque medium, the second after its evacuation, and the third after the insufflation of air. Pictures taken after the administration of certain drugs, such as prostigmine, pituitrin, or atropine, are valuable.

Mild acute sigmoiditis is treated conservatively with antibiotics. Perforation is either sutured or exteriorized, according to the site and gravity of the condition. Sometimes resection may be required. Abscess is evacuated, drained and an artificial anus created.

In occlusive forms colostomy is done without much delay if antibiotics and antispasmodics fail.

As a rule, hemorrhagic forms are treated conservatively, unless suspicion of a neoplasm indicates colectomy.

Tumoral forms require colectomy, performed in one or two stages.

If after exploration acute sigmoiditis without perforation or necrosis is found, colostomy is performed because a tendency to recurrence and occlusion is not infrequently present. At a later date the colostomy is closed or colectomy is performed, according to the roentgenographic findings.

Vesicosigmoid fistulas require the excision and suture of the openings in the bladder and the sigmoid in 2 layers. In complicated cases, colostomy and sigmoidectomy may be required.

No fatalities were recorded among 10 patients operated upon by the authors since the introduction of antibiotics to surgical therapy.

JOSEPH K. NARAT, M.D.

Stricture of the Rectum. A New Treatment. ROBERT TURELL. *Am. J. Surg.*, 1951, 81: 71.

The author established the feasibility and endoscopic electrothermic technique of resection of rectal strictures by means of his recently developed high frequency, double loop resector. He presented an evaluation of the early or short term results of the treatment of (1) benign congenital strictures in juvenile and adult patients, (2) inflammatory diaphragmatic and tubular types of strictures caused by venereal lymphogranuloma, and (3) benign and malignant postoperative strictures following resection and primary anastomosis of the rectum for malignant lesions.

The author believes that if the late results in a large series of treated patients are equally as good, the management of the foregoing types of stricture will be greatly simplified. However, he warned that a final evaluation of this procedure must await a prolonged period of follow-up observation (at least 2 years) as this procedure is still in the experimental stage.

The technique, the preoperative and postoperative management, the instrument, and the histopathologic appearance of the removed specimens are described and profusely illustrated.

Squamous Cell Carcinoma of the Rectum. SAMUEL D. KRON, HAROLD A. WURZEL, and RICHARD J. CHODOFF. *Gastroenterology*, 1951, 17: 194.

The authors present a clinical abstract in the case of a 33 year old negress. On digital rectal examination a firm, irregular fixed mass was found protruding into the rectum posteriorly. On sigmoidoscopic examination, no areas of mucosal ulceration were seen. Biopsy showed extensive squamous cell carcinoma.

Upon operation no gross evidence of metastasis was found. A first-stage Lahey procedure was done. Eighteen days later the second stage of the resection was carried out, including a total hysterectomy and bilateral salpingo-oophorectomy. The patient died about 5½ months after the first operation. No metastasis was found in the inguinal lymph nodes.

RICHARD J BENNETT, JR., M.D.

Use of Sliding Grafts in the Treatment of Anal Fissures. HOWARD K. BELNAP. *Am. J. Surg.*, 1951, 81: 63.

One hundred and ten consecutive operations for anal fissure are reported to have healed with uniformly good results. The operation described in detail consists in the excision of the fissure, including all of the skin covering the sentinel pile, scarred corrugator cutis ani muscle, associated anal papillae glands and crypts, and hemorrhoids in the vicinity. The subcutaneous external sphincter is cut. A triangular area of skin is then circumscribed with a sharp knife, and, without detachment from its subcutaneous tissue, is slid over the defect and sutured to the mucosa at the mucocutaneous junction. The sides are left open for drainage.

The average healing time was 10 days for the anal wound and 20 to 30 days for the donor site. Occasionally sloughing of the inner portion of the graft, formation of an ulcer between the graft and the mucosa, delayed healing due to overlapping of the anal skin, and formation of a granuloma at the donor site occurred. These complications did not materially interfere with a good result.

THOMAS C. DOUGLASS, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Experimental Studies on the Sudden Interruption of the Portal Circulation (Étude expérimentale de l'interruption brusque du courant portal). P. MALLET-GUY, G. DEVIC, M. GANGOLPHE, J. FEROLDI, and M. GRANGEON. *Lyon chir.*, 1950, 45: 929.

The authors have reviewed the literature concerning the effects of complete ligation of the portal vein, and report their experimental work on the dog, which had the objectives of determining the precise mechanism of death after ligation of the portal vein and of finding the best method to prolong the time which the portal vein could be interrupted safely. In 12 animals the survival period varied between 50 and 90 minutes, most of them dying between the fifty-fifth and sixty-fifth minute. The precise clinical records of 1 such animal is reported in detail.

In 4 dogs, biopsies were taken at intervals until the dogs' death; these showed congestion, edema, and then hemorrhage. The arterial pressure was studied in 8 dogs in which the portal vein had been ligated. The curves of these pressures were identical and showed an early rapid fall and then a slow fall, followed by a precipitate drop just before death.

In 3 dogs the portal pressure was found to be between 9 and 11 cm. of water. As soon as the ligature was applied to the portal vein the pressure rose rapidly between 60 and 65 cm. of water. This remained until just before death when the pressure began to fall. The studies of Elman were repeated on 4 dogs and it was found that the animals had lost approximately 50 per cent of the blood mass into their viscera. Studies on the temporary arrest of the portal blood flow were made on 7 animals in which a

clamp had been applied to the portal vein from 18 to 63 minutes. These showed that it was dangerous to interrupt the portal circulation completely for more than ½ hour in the dog. Incomplete obstruction in the portal vein greatly prolonged the survival of these animals.

The re-establishment of the blood volume by transfusions allowed the clamp to be applied for a longer period of time without immediate death of the animal. However, the increased blood volume raised the portal pressure and increased the fragility of the splanchnic capillaries so that the dog eventually died of visceral lesions. A quick temporary anastomosis between the portal vein and the vena cava would be an ideal method of permitting prolonged clamping of the portal vein, but the authors found this method accompanied by too many difficulties to be practical.

Studies on the clamping of the arteries in the portal region led to the survival of dogs for more than twice the 30 minute period previously found safe for clamping of the portal vein. During this time the portal vein could be repaired or an anastomosis could be performed.

THOMAS C. DOUGLASS, M.D.

Benign Stricture of the Common Bile Duct. HARWELL WILSON. *Am. J. Surg.*, 1950, 80: 941.

The primary cause of benign stricture of the common duct is previous biliary tract surgery. Various authorities report its incidence from this cause to be from 75 to 90 per cent. Occasionally, inflammatory conditions in the common duct or inflammatory reaction secondary to a duodenal ulcer may produce common duct stricture.

The prevention of operative stricture of the common duct depends upon good exposure, adequate anesthesia, good light, and careful accurate identification of the cystic and common ducts. The author notes several operative maneuvers which are especially helpful in avoiding damage to the common duct. In the presence of marked inflammatory reaction obscuring the structures he advises removal of the gall bladder from above downward. In the face of severe bleeding, especially from a lost cystic artery, the surgeon must be careful to clamp just the artery. The bleeding may be controlled to accomplish identification of the cystic artery by inserting the index finger in the foramen of Winslow and compressing the hepatic artery between the thumb and index finger. The surgeon should also beware that traction on the cystic duct does not pull up a portion of the common duct which is then mistakenly clamped and ligated.

Types of repair of common duct strictures fall into three groups:

First, those in which end-to-end anastomosis can be accomplished after careful dissection and identification of the ends. This is the most desirable and successful method. Two important suggestions pertinent to this method are: (1) the distal end may frequently be found by rotating the duodenum medially and splitting the head of the pancreas; (2) after anastomosis the "T" tube drain should be inserted through an opening above or below, but never at the site of the anastomotic suture line.

The second type of repair entails anastomosis of a proximal duct stump to the gastrointestinal tract. The author prefers anastomosis between the proximal stump and the jejunum using the Roux "Y" procedure. This method is less likely to be complicated by ascending infection. Accurate mucosa to mucosa anastomosis is essential and is usually best performed over some type of catheter which can be brought to the outside and removed when desired.

The third type of repair involves intrahepatic cholangiojejunostomy with partial hepatectomy, a method recently introduced by Longmire. The author presents the case of a patient who was treated successfully by this method, and who remained free of jaundice or other symptoms for 18 months following surgery. The procedure involves resection of a portion of the left lobe of the liver, by which means the left intrahepatic bile duct is identified and anastomosed to the jejunum, with the use (usually) of a Roux "Y" procedure. FREDERICK C. HOEBEL, M.D.

Diagnostic Morphology of Aberrant Pancreas of the Stomach; Report of 5 Cases. WILLIAM H. BENNER. *Surgery*, 1951, 29: 170.

Five cases of aberrant pancreas of the stomach are described, all of which presented a peculiar and diagnostic alteration of the gastric mucosa consisting of a pseudodiverticulum overlying the aberrant tissue. The presence of the pseudodiverticulum may be accounted for on the basis of a primary anomaly, or it may have been secondary to the presence of the pancreatic tissue. HAROLD LAUFMAN, M.D.

Intrapancreatic Obstruction. CHARLES W. WAINWRIGHT. *N. England J. M.*, 1951, 244: 161.

The natural sequel of intrapancreatic obstruction is increase in pressure in ducts and acini distal to the obstruction. The dilatation of both ducts and acini provides evidence of obstruction, and, when focal in distribution, can mean only that the obstruction is within the gland, and limited to a portion of the gland. The amount of pancreatic juice that escapes into the tissues in and about the pancreas, the concentration of the ferments present, and the chance contact of escaping juice with sizable blood vessels determine the nature and the extent of the damage done. Trypsinogen that escapes into the tissues becomes activated and exerts a specific necrotizing effect upon the blood vessels, the size of the vessel so attacked determining the extent of hemorrhage and the extent to which pancreatic tissue will undergo necrosis as a result of deprivation of blood supply.

The fact that obstruction is the primary factor in producing pancreatic necrosis or hemorrhagic pancreatitis seems inescapable. Although obstruction may be produced in many ways, the existence of intrapancreatic lesions capable of producing this obstruction is the phenomenon that demands atten-

tion. It is not only another cause of pancreatic-duct obstruction, but also the only way in which many hitherto unexplained cases of hemorrhagic pancreatitis can be accounted for. The mechanism first described in the production of acute pancreatitis has so fastened itself upon medical thinking that it has blinded us to the possibility that some mechanism other than biliary tract disease can produce the same condition. That acini rupture far oftener than is realized clinically is evident from the focal fat necroses found at autopsy adjacent to areas of focal acinar dilatation. It is probable that such ruptures often cause no symptoms; at other times they may cause pain that is attributed to something else, or simply not identified. The recognition of these focal acinar ruptures is clinically difficult, and the measurement of serum amylase is the only precise aid available. Already, by means of this test, attention has been called to the probability that obscure upper abdominal pain can be associated with pancreatic disturbance more often than one realizes, and doubtless the recognition of these pancreatic disturbances will become more frequent as time goes on.

BENJAMIN GOLDMAN, M.D.

Acute Pancreatitis with Particular Reference to Its Frequency and to Difficulties in Diagnosis. AARON I. GROLLMAN, GERALD L. BAUM, HAROLD K. MOSS, and SANDER GOODMAN. *Surgery*, 1951, 29: 163.

The incidence of acute pancreatitis is much greater than that which has been reported in recent publications. When blood serum amylase determinations were made in all patients in whom emergency abdominal operations were indicated, 45 cases of acute pancreatitis were diagnosed in a 16 month period in a 250 bed general hospital. Acute pancreatitis may mimic many acute thoracic or abdominal conditions. Inasmuch as there are no definitive signs or symptoms pathognomonic of acute pancreatitis, only awareness of the entity and prompt serum amylase studies will differentiate it from other acute abdominal emergencies.

Of 24 cases with amylase levels of 400 Somogyi units, the roentgenological finding of a sentinel loop of distended small bowel was present in 50 per cent of the cases. This could explain the occasional failure to reveal the site of obstruction at laparotomy performed for acute mechanical intestinal obstruction. It is also important to determine serum amylase levels in thoracic emergencies, inasmuch as there were 6 cases of supposed myocardial infarction and 1 case diagnosed as diaphragmatic pleurisy.

HAROLD LAUFMAN, M.D.

Postnecrotic Pseudocysts of the Pancreas (Pseudokystes post-nécrotiques du pancréas). J. BAUMEL and R. PEDOUSSAUT. *Presse med.*, 1950, 58: 1470.

Four postnecrotic pseudocysts of the pancreas were observed by the authors.

The pain is usually of sudden onset, is violent, of paroxysmal character, and lasts from 5 to 15 hours or even longer; it may be accompanied by rigidity, meteorism, and vomiting, and is located in the epigastric or umbilical region. The pain may radiate toward the left costolumbar region. Signs of pancreatic dyspepsia are absent, or may appear in late stages of the condition.

Loss of weight was noticed in all 4 patients. Pain confined to the region of the pancreas, during the crisis or between the attacks, and not influenced by the position of the patient, is an important diagnostic sign.

Tumefaction in the vicinity of the umbilicus is inconstant and of a transient character.

Duodenal intubation usually fails to reveal significant information. The phosphatase content of the blood is usually increased.

Roentgenographic findings may corroborate the diagnosis. Pseudolacunar image of the major curvature, lowering of Treitz's angle, a filiform appearance of the second portion of the duodenum, and stasis of the third portion suggest the diagnosis of a pseudocyst of the pancreas.

Postnecrotic pseudocysts are sequels of acute or subacute pancreatitis. If sclerotic processes which attempt to reduce the volume of hyperactive lobules are sufficient, scleroatrophic pancreatitis is the result. If they are insufficient, postnecrotic pseudocysts develop.

In order to attenuate the intensity of the secretory reflex, the authors recommend a strict vegetable diet. Atropin may lower the secretion by diminishing the activity of the vagus nerve. If such conservative therapy fails, pancreatectomy should be performed.

JOSEPH K. NARAT, M.D.

GYNECOLOGY

UTERUS

Endometriosis: Clinical Aspects and Therapeutic Considerations. SAMUEL L. SIEGLER and JOSEPH R. BISACCIO. *Am. J. Obst.*, 1951, 61: 99.

In the series here reported, approximately 80 per cent of the patients with external endometriosis were in the age group between 26 and 40 years, and approximately 75 per cent of those with internal endometriosis were in the age group between 36 and 45 years.

The symptoms in all groups were multiple, the most common being characteristically progressive dysmenorrhea, menstrual abnormalities, and low abdominal pain. The most frequent physical findings were cul de sac tenderness and irregularity, palpably enlarged ovaries, tender adnexa (with or without induration), and uterine enlargement, almost invariably due to coexisting fibromas. Prolonged childlessness was frequent in all types.

Treatment was preferably expectant and conservative, especially in young women, with a view to preserving the ovarian and gestational functions. Surgery was resorted to only when the symptoms were uncontrollably progressive in the younger patients; in older women there was no hesitancy about radical procedures, a panhysterectomy being performed whenever possible.

There appeared to be no significant differences in the number of pregnancies resulting from conservative surgery, palliative therapy, or no therapy in women in the same age groups, and the authors found no correlation between the prognosis and the amount and location of endometrial lesions, the postoperative symptomatic relief, and the subsequent pregnancies. ELY ELLIOTT LAZARUS, M.D.

The Management of Fibromyomata Uteri. C. H. MAUZY, F. R. LOCK, and J. F. DONNELLY. *Am. J. Obst.*, 1951, 61: 32.

The express purpose of this article is to evaluate the authors' management of fibromyomata uteri as seen in their own private practice. Treatment was considered radical when the uterus was removed. Conservative measures included simple observation, myomectomy, dilatation and curettage, and irradiation.

Of the 4,077 gynecologic patients studied, 253 had fibroids. Conservative measures were followed in 186 cases. Nearly all (153) of these patients had no treatment other than observation. A small number required dilatation and curettage because of abnormal bleeding. Other presenting symptoms consisted of pain, cancerphobia, leucorrhea, and pelvic pressure. Twenty-seven patients had been advised elsewhere to have a hysterectomy. Eighty-eight patients were followed-up by the authors; the remainder were referred back to their physicians. Only 6 had persistence of symptoms with or without growth of the tumors requiring additional therapy.

Twelve myomectomies, all in the younger women, were done with excellent results in all. The 8 patients who received irradiation (castration) exhibited several common features. They were at or near the menopause, the uterine mass was relatively small, and the main clinical problem was excess and uncontrollable bleeding. Twelve cases associated with pregnancy and 5 with malignancy (1 sarcoma) were briefly mentioned.

On the other hand, hysterectomy was done on 59 patients, and 8 other patients were referred elsewhere for surgery. The majority were subjected to total abdominal hysterectomy and the predominant postoperative complication was urinary tract infection. The predominant clinical features leading to hysterectomy were the presence of a large mass with or without pressure symptoms, excess bleeding, pain, and rapid growth of the tumor. The size of the tumor was usually greater than 5 cm. and not infrequently created the problem of differential diagnosis from an ovarian tumor. After an impartial review of the records of the preceding 59 patients, the authors felt that hysterectomy might have been replaced with a less radical approach in 17 cases.

With Reference to a Case of Malignant Myoma Morphologically Atypical Only in Its Late Metastases (Su un caso di mioma maligno morfologicamente atipico solo nelle metastasi tardive). F. CASSANO. *Riv. ital. gin.*, 1951, 34: 64.

A 30 year old woman was found, on the occasion of the birth of her second child (the first delivery was without abnormality), to have a tumor of the uterus and another in the right inguinal region. The inguinal mass was first noted 4 years previously as a small swelling, hard, mobile, and painless, but during the past 5 months the rate of growth had increased, the tumor attaining the size of a large lemon. The uterine mass when discovered a year previously was fist-sized but had increased in size during the past 5 months to that of an adult head.

Both tumors were excised and provided the histological findings of a pure fibroma. The uterine neoplasm did not recur; however, the inguinal mass did and some 2 years later had again attained a considerable size. This was again removed. At this time there was observed a mass low down on the right side of the mandible and this increased rapidly in size until the patient's death. At this time there was also uncovered, roentgenologically, extensive metastatic involvement of both lung fields.

Histologic examination of the inguinal recurrent tumor and biopsy of the mass on the mandible disclosed in each instance a tumor of fibrous tissues

with, however, indications of a metaplastic transformation toward immature smooth muscle fibers. There was observable also an evident atypical tendency of the cells. The cells were more robust in outline, the nuclei were abnormally formed in places and showed atypical mitoses (triple mitotic figures).

This case is considered by the author to constitute a demonstration of biologic malignancy appearing clinically before evidence of morphologic malignant changes could be determined histologically. The case is also of importance in the matter of the classification of these new growths, in that it constitutes a transitional form between the "pure metastasizing myoma" of Cosia and Tonelli and the group of atypical leiomyomas (malignant myomas of Howells). The case demonstrates more convincingly than any other instance so far reported the ultimate unity of the group of "malignant myomas" (in the broad sense of the term) as proposed by Costa.

JOHN W. BRENNAN, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Puncture of Ovarian Cysts and Cystography (Ponction des kystes de l'ovaire et kystographie). L. PORTES, A. GRANJON, and A. M. BEAU. *Gyn. obst.*, Par., 1950, 49: 422.

Puncture of ovarian cysts through the abdominal or vaginal route has been revived by the authors; they consider it a harmless procedure. Cytologic, chemical, and biologic studies of the aspirated fluid are then made. The method has a diagnostic as well as therapeutic value.

Injection of an opaque medium after aspiration of the fluid allows roentgenographic visualization of the cyst. Direct introduction of the opaque medium into the cyst is less painful and is better tolerated than inundation of the peritoneal cavity by iodized fluid introduced into the tubes. Also, less material is required. The authors employ the same organic iodine compounds as for hysterosalpingography.

It appears that in selected cases injections of iodized material may suppress or retard the growth of ovarian cysts. JOSEPH K. NARAT, M.D.

The Pathology and Clinical Picture of Serous Adenofibromas and Cystadenofibromas of the Ovaries (Zur Pathologie und Klinik der serösen Adenofibrome und Zystadenofibrome des Ovariums). R. J. KLEITSMAN. *Acta obst. gyn. scand.*, 1950, 30: 155.

Two cases of adenofibroma of the ovary, both in women 32 years of age, are reported by the author. In 1 of them the left ovary contained a nodule, the size of an almond, while in the other, a tumor, the size of a hen's egg, was discovered in the right ovary.

In each case the stroma was identical with that of a common fibroma. Both tumors contained epithelial channels and cystic formations of various sizes. The walls of the cysts were lined with a single layer of cuboid or columnar epithelium which bore a close resemblance to the surface epithelium of the involved ovary. The contents of the cysts were serous. The author assumes that the epithelial component of the tumor derived from the surface epithelium of the ovary.

Various terms, such as adenofibroma, fibroadenoma, or adenocystic fibroma of the ovary, have been applied to such formations, which must be differentiated from granulosa cell tumors, Brenner tumors, and teratomas. Portions which resemble adenomas are responsible for a porous appearance of the cut surface of such neoplasms. Two groups may be distinguished: serous adenofibromas which are compact, and cystadenofibromas which are partially compact and in other places contain cysts.

The tumors may attain the size of a man's head or be even larger. The cysts vary in size, while the compact portion is characterized by hard consistency, white color, and lack of elasticity. Ciliary epithelium may occasionally be found in the lining of the cysts. The cytoplasm is granular.

The tumors apparently do not affect the function of the ovaries and the fertility of the bearer. Ascites, torsion of the tumor, and hemorrhages within the tumor may occur.

The clinical symptoms are those of fibromas or adenocystomas of the ovaries.

JOSEPH K. NARAT, M.D.

Secondary Malignant Disease of the Ovaries; A Study of 72 Autopsies. JAMIL KARSH. *Am. J. Obst.*, 1951, 61: 154.

In a study of more than 10,000 autopsies, 72 cases of secondary malignant disease of the ovaries were found. Fifty-three cases were known to be metastatic in origin, while in the remaining 19 cases the secondary invasion was mostly by direct extension, although in some cases the lesion was so extensive that the method of spread could not be ascertained.

The ovaries were not enlarged in about half of the cases, and, therefore, involvement can easily be overlooked at operation. As involvement of the ovaries is important in the prognosis of the primary disease, conclusions drawn from gross inspection of the ovaries is likely to be misleading. The tumors were bilateral in about two-thirds of the cases, and both sides were equally involved in the remaining cases. The microscopic appearance in the large majority of cases was similar to that of the primary lesion.

Pelvic symptoms were overshadowed by those of the primary lesion in most of the cases and ovarian function was rarely disturbed. Detectable ascites was present in half of the cases.

Ovarian metastases occur in the same age group as the primary lesions with one exception: carcinoma of the breast metastasizes to the ovary more often before the menopause.

The primary tumor was most frequently found in the breast (34 per cent of cases), the stomach being the next most common site. Including malignant disease that had spread by direct extension as

well, the cervix was the second most common site of the primary disease. Yet among the cases of carcinoma of the cervix only 3 were metastatic. In a young woman with carcinoma of the cervix the ovaries are rarely involved by metastases. Although carcinoma of the fundus extended to the ovaries in 13 per cent of the cases, only half of the cases were metastatic.

In this series there were 4 Krukenberg tumors, 3 of them with a primary lesion in the stomach and 1 with a primary lesion in the gall bladder.

JOHN R. WOLFF, M.D.

EXTERNAL GENITALIA

The Extended Radical Vulvectomy of Stanley Way. MALCOLM STENING. *Med. J. Australia*, 1950, 2: 823.

The treatment for primary carcinoma of the vulva by radiation or by the so-called radical vulvectomy with superficial gland dissection has been discouraging until recently. The latter operation resulted in a reported 5 year survival of 21 per cent, while the extended radical operation as described by Stanley Way has given a 5 year cure of 83 per cent.

The knowledge of the exact topography of the regional lymph drainage is essential for the understanding of this operation. Although the location of the lesion has a bearing on its spread, carcinoma of the vulva cannot be regarded as a unilateral lesion because the lymphatics of the vulva form a dense and freely communicating network. The regional lymph nodes can be divided into superficial and deep sets, each containing three groups of nodes. The superficial set includes the superficial inguinal nodes lying in the superficial fascia along and below Poupart's ligament, the superficial femoral nodes around the femoral and great saphenous veins in the fossa ovalis, and the presymphyseal nodes in the fatty tissue of the mons veneris. In the deep set are the deep femoral nodes in the superior aspect of the femoral canal above the inguinal ligament, the deep inguinal nodes, an inconstant group lying in the inguinal canal around the extraperitoneal portion of the round ligament, and the external iliac nodes which are situated in a lateral, anterior, and medial group in relation to the external iliac vessels.

Contralateral lymphatic spread is always likely and occurs particularly with the growths of the clitoris or at the fourchet. The size of the primary tumor does not reflect the degree of node involvement. Often, superficial nodes may be by-passed and intrapelvic spread be present.

The extended radical operation for carcinoma of the vulva consists of a wide excision of the vulval region with complete removal en bloc of the potentially afflicted area, its lymphatics, and the lymph node-bearing tissue up to the external iliac nodes.

The incision joins the anterior superior iliac spines across the top of the mons veneris and passes downward to a point below the fossa ovalis on the thigh. From there the incision runs down the inner side of the thigh toward the ischiorectal fossa. The tissues of this entire area are removed in one piece, reaching in depth the external oblique aponeurosis, the rectus sheath, and the fascial coverings of the thigh musculature. The inguinal ligaments on both sides are divided and the external iliac vessels are fully exposed extraperitoneally. Loose areolar tissue and lymph nodes are stripped, beginning at the femoral vessels below the fossa ovalis and reaching up to the external iliacs at the bifurcation. The great saphenous vein is ligated at its entrance into the femoral vein. The vulva is excised with the diathermy knife and hemostasis is obtained mainly by electrocoagulation. The inguinal and femoral canals are closed. The lateral incisions are sutured interruptedly but the excised vulval area is left open. The raw surface is sprayed with a solution of thrombin in saline solution. A Foley catheter is inserted into the urethra. If the urethra is involved it can be resected up to half of its length without causing urinary incontinence. If the anus is involved it should be excised and a colostomy performed.

The operation can be completed in less than 2 hours. Postoperatively, there is remarkable absence of pain and the patient may start walking on the fifth day after the operation. The lower extremities have to be bandaged to reduce edema which is always present and usually lasts for 3 months. The inguinal incisions heal by primary intention in 7 or 8 days. Healing of the raw surface of the vulval area requires 6 weeks or more because of the unavoidable secondary wound infection. Skin grafting is not advisable because of the poor results in this area. In elderly women, dry methods and wound treatment appear more satisfactory. The ultimate cosmetic and functional result of this operation is satisfactory, giving a very good prognosis for the cure of the malignancy.

Eight patients, aged 65, 72, 81, 76, 75, 70, 68, and 53 years, have been operated upon by the author by this technique since December, 1949. There has been no primary operative mortality. One patient, 81 years of age, died 3 months after her discharge from the hospital with a terminal pulmonary condition with hemoptysis. Four of the patients were in a very advanced stage. In 5, there was lymph node involvement. In 1 patient the lower half of the urethra, and in another the anus, had to be resected. In 2 patients, the groin wounds did not heal by primary intention. HERBERT TEICHNER, M.D.

MISCELLANEOUS

The Experimental Production and Prolonged Maintenance of Decidua in the Nonpregnant Woman. EDUARD EICHNER, GEORGE G. GOLER, JOHN REED, and MAURICE B. GORDON. *Am. J. Obst.*, 1951, 61: 253.

Eight patients at the Cleveland State Hospital were subjects in the research problem of producing by hormones the pyeloureteral dilatation so common in pregnancy. At the start of the experiment all were normally menstruating women of childbearing

age. Four were parous and 3 were virginal. Pelvic examinations disclosed no gross abnormalities, and preliminary endometrial biopsies verified ovulation. Therapy was started on all patients on the same date, the phase of the menstrual cycle being disregarded. Cervical and vaginal spread, catheterized bladder-urine sediment, blood counts and blood chemistry endometrial biopsy, and 24 hour urine examinations were made at intervals. Culdoscopic examination of the ovaries was also done. Clinical signs of early pregnancy (amenorrhea associated with uterine and breast changes and a positive pregnancy test) were observed in each subject.

Each patient received 275 mgm. of estradiol by pellet implantation and 12,875 mgm. of progesterone by injection. Half of them received chorionic gonadotropin during the first two-thirds of the experiment. The others received up to a total of 282,000 units.

Endometrial biopsies proved the presence of a pseudopregnancy reaction with the formation of a decidual endometrium in all cases. The response persisted for more than 5 months and required all three hormones for its maintenance.

JOHN R. WOLFF, M.D.

Male Pseudohermaphroditism: Some Endocrinological and Psychosexual Aspects. E. C. HAMBLEN, F. BAYARD CARTER, JAMES T. WORTHAM, and JUAN ZANARTU. *Am. J. Obst.*, 1951, 61: 1.

Through the technique of endocrine evaluation, the authors show that it is possible to arrive at a more or less accurate scientific conclusion as to the sex to which male pseudohermaphrodites really belong, and then to proceed by surgery and by therapy to accent the characteristics both physical and physiological to a degree which may permit them to assume a definite status in life.

Studies of 11 male pseudohermaphrodites from the standpoint of histopathology of the testes, levels of urinary gonadotropins and 17-ketosteroids, and psychosexual orientation are reported. Particular attention is paid to the patients with gynecoid psychosexual patterns. The results of castration and estrogenization of these patients, and the response of local target organs to estrogen therapy were considered. Justification for the castration of these individuals, and the beneficial effects of estrogenization were discussed, as well as the sociological and medicolegal questions posed by these patients. From the standpoint of psychological expediency and clinical practicality, the correct sex is that which the individual desires and to which there is orientation.

CHARLES BARON, M.D.

Clinical Types of Genital Prolapse and Choice of Curative Surgical Technique (Formes cliniques des prolapsus génitaux et choix de la technique chirurgicale curatrice). E. HERVET. *Gyn. obst.*, Par., 1950, 49: 459.

The author deals not with the surgical technique but with the indications for the various interventions in genital prolapse.

There are numerous anatomoclinical varieties of prolapse, each requiring a different surgical approach. The employment of anterior colporrhaphy and posterior colpomyorrhaphy in each case must unavoidably lead to recurrences.

Hysteropexy alone is apt to be followed by a recurrence in the form of a hernia through Douglas' pouch.

Three groups of patients with prolapse may be distinguished: (1) those in the childbearing age, (2) those in the menopause who wish to preserve their vagina, and (3) those who intend to refrain from sexual relations.

In the last-mentioned group total or subtotal colpectomy, with or without hysterectomy, is the best procedure.

In women of childbearing age classical colpoperineorrhaphy is employed if no retroversion, hypertrophic elongation of the cervix, or incontinence is present. Retroversion is corrected by Crossen's operation or vesicofixation.

In the second group classical perineorrhaphy is performed if the uterus is in the position of anteversion. Retroversion requires vesicovaginal interposition of the uterus. Pathologic conditions of the uterus are eliminated by reconstruction of the pelvic floor according to Campbell's technique.

JOSEPH K. NARAT, M.D.

The Etiology, Diagnosis, and Surgical Treatment of Female Sterility. AXEL WESTMAN. *Acta obst. gyn. scand.*, 1950, 30: 186.

A series of 1,402 cases of female sterility in which there was no evidence of endocrine disturbance is discussed; 93 per cent of the cases were followed up. In 959 cases there was primary, and in 443 secondary, sterility. The ages of the majority of the patients ranged between 25 and 34 years. In 378 cases the patient was older than 35 years. The duration of the sterility was approximately 4 years in the majority of cases.

In 398 cases, or 28 per cent, no abnormality was found. In 633 cases, or 47 per cent, there was evidence of sequelae of adnexitis; the cause of the primary infection was unknown in most of these cases. The high incidence of tuberculous salpingitis was remarkable (58 cases, or 11 per cent). In 317 cases, or 23 per cent, there was evidence of abnormal conditions in the uterus. In 24, or 2 per cent, abnormal conditions were present in the vagina and vulva.

The therapeutic results were as follows: of 1,402 patients, 389, or 28 per cent, became pregnant. In 329 the pregnancy progressed normally, but in 60 it resulted in abortion. Of the 389 patients who became pregnant, 272 were examined only by salpingography and diagnostic curettage. This is evidence that diagnostic procedures are of great therapeutic value. In 614 cases the patient was treated by operation and pregnancy ensued in 19 per cent of these.

The indications for operative measures are discussed in considerable detail. Suggestions to improve the operative methods are offered with special

consideration of those employed for the repair of occluded tubes. The author suggests that special clinics for the treatment of sterility be established and emphasizes that the most important step in the fight against sterility is rational prophylaxis.

CHARLES BARON, M.D.

The Biologic Action of Prolactine. Findings on the Uteri of Guinea Pigs Treated with Estrogen and Prolactine (L'azione biologica della prolattina. Rilievi su uteri di cavie trattate con estrogeni e prolattina). P. CATTANEO and M. RUSSO. *Clin. ostet.*, 1950, 52: 261.

Prolactine is a proteohormone of the anterior hypophysis. The hormone is closely related, as far as concerns its derivation and chemical constitution, to the growth hormone of this organ. In fact, the lactopoetic action attributed to prolactine is, in the authors' opinion, to be ascribed to an admixture (impurities) of the growth hormone itself, whose lactopoietic properties have already been demonstrated by Cotes and his coworkers (*Nature*, 1949, 164/4180: 992–993). The effects of prolactine itself are believed to consist in antifolliculin and luteotrophic actions. It is the latter properties which the authors have purposed to investigate.

Twelve female guinea pigs of the same family and of approximately the same body weight (350 gm. ± 20) were selected. These animals were in the same phase of estrus (open vagina), so chosen with the idea of initiating the experiments during the same period of the sexual cycle (2 days after closure of the vagina). Two of these pigs were untreated (controls) and the remaining animals were injected exclusively with prolactine (lyophilized hormolactine, Richter), with estrogen (dihydrofolliculin dipropionate, Richter), or with prolactine and estrogen combined. The animals were then sacrificed, the sexual tract was removed and photographed, and sections for microscopic study were made transversely through the left uterine cornu of each animal, about 4 cm. from the ovary.

The findings were sufficiently consistent with this method to indicate that prolactine exercises an antagonistic effect toward the estrogen employed. With constant dosage of the estrogen (28,000 to 42,000 U. I.) increasing amounts of the prolactine (starting with 10 U. I. daily for 14 days consecutively) would lead to the point where the prolactine would cause the usual endometrial congestion, necrotic areas, and bleeding, which were observed in the animals under the influence of such large dosages of estrogen. In fact, with very large dosages of prolactine (50 U. I. daily for 14 days) there seemed to be not only a suppression of the estrogen administered by injection, but also a suppression of the normal, physiological estrogen from the animal's own ovary (pseudopregnancy).

From their experiences the authors conclude that it is the physiological prolactine which protects pregnancy by its luteotrophic effect, suppresses oogenesis, and maintains the physiologic amenorrhea during the puerperium. They also believe that their results are sufficiently encouraging to justify the use of prolactine clinically in the conditions characterized by hyperfolliculinemia.

JOHN W. BRENNAN, M.D.

The Frequency of Micro-Organisms Resistant to Antibiotics and Sulfonamides (Die Haeufigkeit resistenter Keime gegen Antibiotika und Sulfonamide). J. H. NAPP and J. CLAUSS. *Geburtsh. & Frauenh.*, 1950, 10: 799.

The results of in vitro tests of sensitivity of staphylococci, streptococci, enterococci, and Escherichia coli to penicillin, streptomycin, and aureomycin corresponded to the effectiveness of these antibiotics in patients. Similar tests pertaining to sulfonamides furnished reliable results when Escherichia coli or enterococci were studied, but the tests proved to be less valuable when staphylococci were examined.

Testing the sensitivity of micro-organisms responsible for puerperal or gynecologic infections is as important as determination of the species.

Penicillin resistant staphylococci were found in 39 per cent of the patients with mastitis, 50 per cent of those with pyelitis, and 17 per cent of those with puerperal infections.

Staphylococci and gonococci show a tendency to develop resistance to streptomycin but not to aureomycin. Smears of nasal discharge from 38.5 per cent of all physicians and 75 per cent of all nurses contained penicillin-resistant staphylococci.

Ointments containing aureomycin are best suited for the prophylactic treatment of mastitis.

Enterococci were sensitive to aureomycin and usually showed resistance to penicillin, streptomycin, and the sulfonamides.

The authors recommend in vitro tests for the selection of the best antibiotic or sulfonamide for the treatment of puerperal or gynecologic infections.

JOSEPH K. NARAT, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Observations on the Use of 10 Per Cent Salt Free Macrodex (Dextran) in Toxemia of Late Pregnancy. PAAVO VARA. *Acta obst. gyn. scand.*, 1950, 30: Supp. 6.

Macrodex, a polysaccharide built up from glucose molecules, has been used in the Scandinavian countries as a substitute for plasma in many experimental studies. The macrodex molecules are large enough not to penetrate through the vascular walls of the blood vessels, but remain in the blood circulation and thus increase the volume of circulating fluid. For this reason this substance has been used in shock and other conditions in which an increase in colloid-osmotic pressure of the plasma is desired.

The purpose of this study has been to explain the effects of the use of 10 per cent salt free macrodex in the treatment of toxemia of late pregnancy. Three of the 21 patients in this series had slight toxemia, 15 had pre-eclampsia, and 1 patient had essential hypertonia complicated by toxemia of late pregnancy. Each patient was treated with from 1 to 7 bottles (each containing 500 ml. of macrodex). In connection with the macrodex treatment, the fluid balance of the body was also under observation, and the hemoglobin value, the erythrocyte count, the hematocrit value, the serum protein percentage, and the sodium chloride in the whole blood and its serum were determined. The sodium chloride in the daily output of urine was estimated for 2 days, in connection with the other studies. The alkali reserve and the urea of the blood were also estimated.

In 7 cases the disappearance of macrodex from the blood was tested by the Hint-Thorsen method. The macrodex concentration of the blood fell quite sharply and none of it was traceable on the third day after its administration. Tests made on specimens taken from the umbilical cord of the newborn infant showed no traces of macrodex in any of the cases, which proved that the macrodex did not enter the circulatory system of the fetus.

The administration of macrodex had a favorable effect on the condition in all of the cases, causing a rise of the urine output, a fall in the blood pressure, and cure of the acidosis. Following the fall immediately after the administration of macrodex, a rise was noted in the protein percentage after 1 or 2 days. The subjective symptoms disappeared also in most of the cases and the patient made a good recovery. Reduction of the increased hemoconcentration was not clearly observable in all of the cases from the laboratory tests, since the figures of the blood studies were often affected by the larger or smaller loss of blood which always occurs during delivery.

The favorable effect of macrodex in toxemias of late pregnancy helps to prove that these conditions, which are accompanied by a reduction of the colloid-osmotic pressure, call more naturally for the kind of treatment that raises this pressure rather than a type which reduces it, such as venesection.

Subsidiary effects were noted in 2 cases, but they were due to too rapid infusion, because no by-effects were noted later when the infusion was carried out more slowly, by drops. As macrodex is eliminated fairly rapidly from the circulatory system, the infusion should be renewed approximately every second day for a continuous effect, to keep the colloid-osmotic pressure of the plasma at as high a level as possible. ELY ELLIOTT LAZARUS, M.D.

The Management of Pregnancy and Labor in Diabetes Mellitus. (Schwangerschaft und Geburtsleitung bei Diabetes mellitus). GEORG HOERMANN. *Deut. med. Wschr.*, 1950, 75: 1741.

Among the 25,210 deliveries which occurred from 1934 to 1939 at the Women's Hospital of the University of Kiel, there were 20 patients with diabetes, an incidence of 1 to 1261. There was 1 maternal death (5%) in a 40 year old gravida-iv, para-ii, in whom the diabetes was not discovered until near term when she first came to the clinic. Eight infants (40%) died, of which 2 were premature, weighing 920 and 1,650 gm., respectively.

If the disease is discovered and its treatment initiated before the beginning of pregnancy, the outlook for the mother and infant is altogether better. As a rule, the diabetes will respond to insulin. Of the 15 patients in this group, all of the mothers and 9 of the infants survived. It is much more difficult to control the diabetes if it is first discovered during pregnancy. There is a greater tendency toward diabetic coma and the response to insulin is often poor or altogether absent. Two patients were in this group; 1 of them died 20 hours postpartum in diabetic coma and both of the infants were lost. A third clinical type is that of latent diabetes which may be diagnosed only by sugar tolerance tests. Although diabetic complications do not occur, it is of obstetrical importance because it may produce either premature or overly large infants, as well as stillbirths and neonatal deaths. Three cases were in this group without a maternal death. However, 1 infant, 56 cm. in length and weighing 6,050 gm., died during the delivery.

Infants of more than 4,000 gm. were observed in 9 instances, and 2 of these, including the 1 mentioned, died. The danger of postmaturity lies mainly in the possible fetopelvic disproportion. Only 1 baby who died had a congenital abnormality, consisting of a defect in the intraventricular septum. The principal danger for the newborn infant is the appearance of hypoglycemia, which is attributed to hyperplasia of the infant's pancreas.

There were 5 patients with pre-eclamptic toxemia and 2 with eclampsia. Primary uterine inertia occurred in 9 cases. The only cesarean section in this

series was a repeat section for which, however, the main indication was given as uterine inertia and uncontrollable diabetes.

The importance of good prenatal care is stressed. Particular attention is to be given to a diet and the coverage of carbohydrates with insulin.

HERBERT TEICHNER, M.D.

LABOR AND ITS COMPLICATIONS

An Analysis of 10 Years of Cesarean Section at the Cincinnati General Hospital. ROBERT W. KISTNER. *Am. J. Obst.*, 1951, 61: 109.

A survey of 251 cesarean sections occurring during the interval from 1940 to 1949 is presented. The over-all incidence of sections is 1 per cent of the total number of deliveries. The incidence was twice as high in the negro as in the white race.

The chief indications were cephalopelvic disproportion, repeat sections, and hemorrhage. New indications during the last 2 years have been preeclampsia and uterine inertia. An increasing number of the laparotrachelotomy type of sections are being performed both in clean and potentially infected cases. The classical section should be relegated to the clean case in which fetal or maternal life depends upon haste. There has been a marked trend, recently, toward the use of regional anesthesia, chiefly spinal, for cesarean section. Extreme care and low dosage are necessary adjuncts to this method. The morbidity rate was 43 per cent. During the last 5 years, penicillin, sulfonamides, aureomycin, blood, and oxygen have been utilized to diminish the morbidity. The chief complications were wound breakdown and pulmonary disease.

The gross fetal mortality rate was 5.1 per cent and the corrected rate was 2.3 per cent. A diminution in the over-all fetal mortality rate has been shown to accompany the increased incidence of cesarean section. The fetal mortality rate in cesarean section was one-tenth of that obtained with the hydrostatic bag and one-third of that associated with high and midforceps during the same period. The maternal mortality rate was 1.1 per cent. Anesthesia accounted for all 3 maternal deaths. From a study of the mortality figures it is apparent that during the past 10 years it has not been more hazardous for the mother to be delivered by cesarean section than by operative vaginal procedures.

ELY ELLIOTT LAZARUS, M.D.

Conduction Anesthesia in Obstetrics. Caudal Anesthesia, Lumbar Peridural Anesthesia, and Bilateral Lumbar Sympathetic Block with Single Doses of Xylocaine in 231 Deliveries. LARS RISHOLM. *Acta Soc. med. Upsaliensis*, 1950, 55: 323.

It is a well known fact that the intensity of pain in childbirth varies greatly for different women. At present it is believed that distention of the lower uterine segment is responsible for the main part of labor pains, and not the contraction of the uterine muscle. In the second stage of labor, distention of the vagina and perineum is an additional cause of pain.

The possibilities of alleviating pain during delivery with conduction anesthesias have long been known and many different methods have been tried. As compared with other forms of anesthesia in delivery, conduction anesthesia has the advantage that one need not reckon with any effects of the anesthetic upon the child. Spinal and continuous caudal anesthesia have been the most predominant methods of conduction anesthesia.

From a study of 231 cases reported, the author concludes that single, and at times repeated, caudal injections may yield good results, provided that with this method a long acting anesthetic be used. The author employs 2 per cent xylocaine. A marked disadvantage, especially in primipara, is a prolongation of the second stage of labor. From experiments the author has conducted, he concludes that with lumbar peridural anesthesia and bilateral sympathetic block a good analgesia is obtained during the greater part of the delivery without any effect upon the normal course of the delivery. He recommends a selective and combined use of these three methods.

ELY ELLIOTT LAZARUS, M.D.

NEWBORN

Erythroblastosis Fetalis. Treatment with Exchange Transfusion. LOUIS K. DIAMOND, FRED H. ALLEN, and WILLIAM O. THOMAS, JR. *N. England J. M.*, 1951, 244: 39.

Exchange transfusion is the treatment of choice for babies with erythroblastosis fetalis, because it has been shown that its use has brought about a decrease in mortality, along with a marked reduction in the incidence of kernicterus.

The technical details of a method of exchange transfusion through a single plastic tubing, inserted into the umbilical vein, are presented, as well as an outline for aftercare.

Exchange transfusion is done immediately under the following conditions:

1. If the baby (less than 24 hours of age) has clinically apparent erythroblastosis fetalis on the basis of early jaundice, hepatosplenomegaly, pallor, edema, or petechiae, or a red cell count of less than about 4,500,000 with a hemoglobin value of less than about 13.5 gm. per 100 c.c.

2. If the baby is Rh-positive, as demonstrated by direct testing or a positive direct Coombs test, and the mother's titer of Rh antibody was 1:16 or higher at some time during pregnancy. It must be remembered that about 10 per cent of erythroblastotic babies are typed as Rh-negative by all the usual typing methods when they should be typed as Rh-positive. A positive direct Coombs test indicates indirectly that the baby is Rh-positive when the mother's serum is known to contain Rh antibodies.

3. If the baby is Rh-positive and there is an unfavorable past history, particularly a history of ker-

nicterus in a previous sibling, regardless of the titer level. This criterion is based on the conclusion that kernicterus is preventable in some, if not in all, cases by exchange transfusion. Exchange transfusions have been done in babies who already had signs and symptoms of kernicterus without apparent benefit, but it is not certain that exchange transfusion may not be beneficial to some babies with early signs of kernicterus.

4. If the Rh-positive baby is immature, for example, a baby with an estimated gestation of less than 38 weeks. This criterion is based on the likelihood of kernicterus in immature, especially in immature male, babies.

A second exchange transfusion is given, 12 to 24 hours after the first one, whenever the likelihood of kernicterus seems high.

CHARLES BARON, M.D.

MISCELLANEOUS

Clinical Report of the Rotunda Hospital. *Irish J. M. Sc.*, 1950, 6: 1.

During the year, 4,305 women were admitted to the labor wards of the Rotunda Hospital and 3,928 women who were more than 28 weeks' pregnant were delivered. There were 9 maternal deaths, 4 of the women being undelivered.

A small postpartum toxemia clinic has been established.

All women admitted to the maternity wards have their blood tested for the Rh factor.

Early ambulation is carried out in both maternity and gynecologic departments. No ill effects, nor opposition from patients, have been encountered. Except in the presence of some serious condition contraindicating early rising, maternity patients walk about from the second puerperal day, and are allowed to go to the lavatories on the fourth day. This has greatly reduced bedpan duties, but has necessitated the installation of additional lavatories. The incidence of saphenous thrombosis and phlebitis appears unaltered, but there have been no cases of pulmonary embolism.

Pentothal with curare and cyclopropane is used for gynecologic work, and pentothal with curare and gas oxygen for cesarean sections. Pentothal induction followed by gas oxygen is routine for examinations when delivery is not imminent. An analgesia service has now been extended to the patients' own homes.

Early transfusion therapy is being used on Rh babies. Maternal whole blood is given intramuscularly as a routine at delivery in cases of proved or suspected cerebral hemorrhage. Both the incidence and severity of intracranial lesions appear to be lessened.

The hospital is sadly handicapped by the lack of prenatal beds, of which there are only 8. At least 20, preferably 30, such beds are needed. Because of this shortage, proper treatment is refused many patients requiring prenatal care.

Of the 3,928 women delivered in the hospital at more than 28 weeks, 85.5 per cent (3,360) received antenatal care. Similar care was also given to 63 per cent of the 1,790 women attended in their own homes.

Twenty-seven women suffering from active pulmonary tuberculosis, and 66 whose condition was described as "highly suspicious," were delivered. Only 1 case of active pulmonary tuberculosis was discovered among the 102 women x-rayed in the hospital, and it is disappointing that only 593 of the 3,471 antenatal patients advised to attend the Mass Radiography Center availed themselves of this opportunity. A portable x-ray unit might solve this problem.

The number of blood donors was 290, and 85 transfusions were given, a considerable increase over the previous year. There were 4 slight reactions, and no deaths directly attributable to transfusion.

Both British Medical Association and Rotunda Hospital standards of morbidity are observed. There has been no change in treatment of puerperal infection; early rising out of bed is routine; sulfathiazole and penicillin are used as before, and cervical smears are taken when there is a temperature of more than 99 degrees.

There were 164 morbid cases. As in previous years, the morbidity distribution according to frequency of the different groups of organisms was coliform, staphylococci, mixed growths, and hemolytic streptococci. There were very few persistent fevers, and only 3 women were detained in the hospital longer than 30 days. No case of puerperal pyrexia was referred to another hospital, and there were no deaths from puerperal fever. The incidence of hemolytic streptococci infection among morbid patients was double that of last year, or 6.7 per cent.

Although fetid lochia occurred, neither this nor subinvolution appear as important as in the pre-sulfonamide and penicillin era. The greatest number of cases of morbidity were observed during the months of November, December, and January, and the predominant organism over this period was the hemolytic streptococcus.

Sulfathalidine has been used routinely for pyelitis complicating pregnancy and the puerperium. There have been no difficulties resulting from this treatment, and the response has been satisfactory.

Where cardiac disease complicated the pregnancy, 17 cases were attended without a maternal, and with only 1 fetal, death. The fetal death was without obvious cause. It is the policy to avoid any interference during labor, which should be allowed to begin spontaneously, and only to assist in such cases when the progress of labor ceases. Prolonged rest in bed is essential prior to confinement. The 17 cases represent an incidence of 0.43 per cent, and were classified as follows: grade 1, six cases; grade 2, seven cases; grade 3, two cases; grade 4, two cases. In all instances, either gas oxygen or open ether was used for the delivery, and in none of the patients was there cause for grave anxiety.

Thirty-two patients with hypochromic anemia were treated with intravenous injections of iron. Six injections are given to each over a 10 day period. Their hemoglobin increased from an average of 37 to 45.6 per cent. The response has been best in postpartum cases. It is given routinely when the hemoglobin is less than 40 per cent.

In the third stage of labor the dorsal position, with nonintervention until the placenta is in the vagina, is kept unless there is a hemorrhage or the placenta is retained for 1 hour or more.

Forty-one patients (1.04%) required manual removal, as compared with 35 in the previous year. In none was ergometrine nor any other oxytoxic drug given until the third stage of labor was completed, and there was no maternal death. The average total blood loss in this manual removal was 16 ounces, and the average duration of the third stage was 45 minutes. The longest delay was 5 hours; in 2 cases, manual removal was performed immediately following delivery because of violent hemorrhage. The greatest blood loss was approximately 2 pints; only 4 transfusions were necessary, but intravenous glucose was given freely. Gentle Crede expression under anesthesia is attempted, provided no shock is present. No ill results have been noted.

There were 49 cases of placenta previa, with 1 maternal death, 13 stillbirths, and 1 neonatal death due to prematurity. There were no serious puerperal complications in the cesarean section group, and only 1 classical section was performed.

Analysis of the different methods of delivery shows that cesarean section was used 22 times; puncture of the membranes alone, 5 times; Braxton Hicks version and/or bringing down the leg, 7 times; forceps (to complete delivery), 6 times; no treatment other than observation, 9 times. Treatments other than cesarean section were confined to patients with very minor degrees of placenta previa, and to those in whom delivery was hopelessly premature.

The routine treatment for placenta previa is as follows: when the patient is in good condition and there is no further bleeding she is required to rest for 48 hours before being examined internally. During this time her blood group is determined, and the advisability of blood transfusion before examination is considered. Internal examination is carried out only in the operating room with everything ready for cesarean section. The lower segment technique is used unless there are large lower segment sinuses or dense lower abdominal adhesions from a previous operation, and all cases of placenta previa are delivered thus unless the pregnancy is of less than 32 weeks, the degree of previa slight, and the woman's condition exceptionally good.

There is no accepted standard of pregnancy toxemia, and for this reason the incidence of toxemia and the results following different treatments cannot be assessed with accuracy.

There were 128 cases of pregnancy toxemia, including chronic nephritis and essential hypertension, 78 occurring in primigravidas. The average parity was 2.9, the average age was 33.7 years, and the highest blood pressure, 260/156. The forceps were necessary in 33.6 per cent, and abdominal delivery was performed in 9.3 per cent. Labor was induced in 51 women at an average period of pregnancy of 37.8 weeks, and the weight of the babies averaged 6 lbs., 8 oz. The stillbirth incidence was 5.8 per cent. There was 1 maternal death. Slightly better results were obtained in the more severe toxemias, treated by premature induction of labor in the milder group which was allowed to go to term. The fact that the babies were heavier in those cases in which pregnancy was terminated before the thirty-eighth week supports the belief that carrying the pregnancy to term favors loss in fetal weight in utero, and a higher fetal death rate. Treatment of pregnancy toxemia is concentrated on absolute rest, with complete starvation and restricted fluids, for at least 48 hours. Sedatives are used in mild cases; in the more severe cases, with any suggestion of threatened cerebral complications or convulsions, morphine sulfate, one-sixth grain, is used every 6 hours. Edema is harmful, not only generally, but possibly to the retina and the cerebral cortex, and when it is present an attempt is made to remove it by limiting the further intake of fluids. A total not to exceed 2½ pints of fluid per 24 hours is given intravenously, all fluids by mouth being withheld until free bowel action is established. In some instances 20 to 30 ounces intravenously may be ample daily. Unless the output of urine is at least 1 ounce or more, one pint of 20 or 30 per cent pure dextrose solution is given intravenously at intervals of 8 hours, to promote diuresis. With lessening weight and the bowels acting freely, oral fluids are substituted gradually for intravenous fluids, but if this is followed by any sign of return of the edema the pregnancy should be terminated. The routine must be continued after delivery in all eclamptics and pre-eclamptics.

The following are important indications for immediate termination of pregnancy: (1) failure to respond to edema reduction therapy, as evidenced by poor response to intravenous concentrated glucose; (2) a blood pressure persistently over 160 systolic, or steadily rising; (3) the development of retinopathy; (4) severe headache, with or without epigastric pain or jaundice; (5) diminishing urinary output and increasing albuminuria, especially if the urinary output is less than the arbitrary 1 ounce per hour; (6) restlessness or irritability despite sedative treatment, suggesting the likely onset of convulsions.

There were 9 cases of eclampsia with 1 maternal death (a primigravida), 3 stillbirths, and 2 neonatal deaths. Seven patients had received antenatal care, and the 1 maternal death was in this group. Four pregnancies were terminated by forceps, 2 by cesarean section, and 3 by spontaneous delivery. Apart from the usual clinical signs and symptoms, no association of facts can be isolated from a study of the fatal case, but antenatal supervision seems to be a poor safeguard against fulminating toxemia. In eclampsia, the same pure concentrated glucose intra-

venous therapy was followed with strictly controlled fluid intake routine, coupled with continuous oxygen administration and pentothal following an initial dose of morphine to prevent convulsions. The maternal mortality of 11.1 per cent in such a small number of eclamptic cases is inconclusive and cannot be viewed with complacency.

Accidental hemorrhage occurred in 38 cases. Not more than half the so-called toxemic accidental hemorrhages have any toxemic background but are, in fact, only pseudotoxemias because of the temporary albuminuria. The routine treatment consists of bedrest, moderate warmth, intravenous glucose and morphine, with half-hourly observation of blood pressure, pulse, and temperature. Urinary output and the albumen blood content is carefully noted. When the patient's condition has improved and her blood pressure and warmth are restored, the membranes are punctured and pitocin is given in ¼ c.c. doses half-hourly, unless labor is present. When shock is deepening and labor absent, laparotomy with cesarean section, and possibly hysterectomy, is advised. The value of blood transfusion is doubtful unless there has been exceptionally severe bleeding. Continuous oxygen is important.

In 95 cases, labor lasting 48 hours or more occurred without a maternal death; 78 of the patients were primiparas. There were 11 stillborn infants and 4 neonatal deaths. In 23 women, delivery was spontaneous. Cesarean section was employed in 8 cases and 2 patients were delivered by breech extraction. Seventeen patients were morbid, 14 following forceps delivery, 2 following cesarean section, and 1 subsequent to spontaneous delivery. Pitocin-glucose drip treatment was used 11 times, with good effect in 7 cases, and without effect in 3. With fetal distress in 1 case, and the formation of a contraction ring, cesarean section was done. Although of definite value in carefully selected cases, the pitocin drip treatment should never be allowed to displace patience, and the use of lower segment section when necessary.

Delivery by forceps was necessary in 412 women (incidence 10.4 per cent), with 22 fetal deaths. Although the incidence of delivery by forceps is slightly less this year than last, it is believed there is often too great a delay in their use; fetal distress, due to delay in the second stage of labor, should never be allowed to develop. The arbitrary time limits for so-called "delay" in the second stage should be abolished, and forceps delivery should be routine when advance ceases, even though neither fetal nor maternal distress are present.

Primary occipitoposterior position was encountered in 140 patients. Anterior rotation was successfully accomplished in 24 cases, in which Kielland's forceps was used 13 times.

Breech presentation occurred in 215 cases. Unless the fetus turns easily at the thirty-sixth to the thirty-seventh week, persistent efforts are not made at external version. If there are doubts about disproportion, x-ray pelvimetry is used and an assessment is made of the future course to be taken. In doubtful cases of disproportion in elderly primiparas cesarean section is employed. Local anesthesia infiltration with episiotomy is frequently used for second-stage delay in breech labor, rather than forceps.

Thirty-seven women who had had previous cesarean sections were delivered vaginally.

Medicinal induction of labor is unreliable. If induction of labor is to be more certain, low puncture of the membranes must be combined with the medical technique.

Cesarean section was performed in 113 cases (2.8%). There were 109 lower segment operations (68 repeat and 41 new) and 3 new classical operations. The morbidity rate was high at 17.8 per cent, including 1 classical operation. Hysterectomy was done 6 times immediately following lower segment delivery, and all these women recovered. There was 1 maternal death (0.89%) with a stillborn infant. The fetal mortality rate was 3.57 per cent.

One hundred and six cases of disproportion (2.73%) were encountered. There were no maternal deaths but there were 6 stillborn infants and 1 neonatal death. CHARLES BARON, M.D.

Placenta Accreta. Considerations with Reference to a Case of Placenta Previa Central, Accreta and Diffusa (Placenta accreta. Consideraciones sobre un caso de placenta previa central, accreta y difusa). D. EMILIO GIL VERNET, J. PÉREZ SOLER, and J. ESTEBA CABALLERIA. *Acta endocr. gyn.*, Porto, 1950, 3: 534.

The 34 year old patient had given birth to 3 normal children at term; the fourth gestation ended as an abortion at 6 months; the present pregnancy was the fifth. In all these births the placenta had had to be removed manually because of hemorrhages and lack of spontaneous expulsion.

The present labor began as a vertex presentation with the back to the right. The uterus went into spasm and vaginal examination showed a dilating cervix and, impeding the insertion of the finger, an obtruding mass like a cushion, which was holding up the descent of the presenting part. This digital exploration gave rise to an important hemorrhage (about 400 c.c. of blood). There had been no bleeding during the gestation.

At celiotomy, during incision of the lower uterine segment, the uterine wall was found to be abnormally thin, the umbilical cord led upward in the direction of the uterine fundus, and the entire inner surface of the uterine cavity was covered by a thin placenta which was so intimately adherent as to render separation in the normal sense impossible; attempts to pull loose the thin placental organ resulted in the separation of fragments, taking with themselves fragments of the muscular wall.

Subtotal hysterectomy was done, only a small portion of the cervix being left, peritonization was rapidly carried out, and the wound was closed in layers. Blood (1 liter) was transfused preoperatively and during the operation, and heart tonics and physiologic saline solution were given; however, the patient died an hour later and the child could not be revived.

Anatomopathologic and histologic examination of the removed specimen disclosed the direct invasion of the muscular walls by the chorionic villi, without the interposition of any adequate quantity of decidual tissue. The muscular cells about the area of chorial penetration evidenced breaking down with necrotic and hyaline changes, apparently analogous to the changes in the decidual tissues in normal pregnancy. The chorionic villi themselves were found to contain abnormally large amounts of cells, resembling the earliest stages of the syncytial cells, the normal products of conception. Interspersed were areas of cells resembling the earliest stages of Langhans cells.

From this evidence of fetal morphologic persistence of the syncytial and Langhans cells the authors postulate the persistence also of the biologic activity of the amniotic sac, resulting in the abnormal attack on, and irregular thinning of, the uterine muscular walls. In support of this contention of the predominance of the fetal factor in these cases, the authors present here a second time a previously reported instance of implantation in a uterine horn with invasion of the muscular wall and actual perforation of the uterus at this point. In this area of the uterine cavity the deciduum is always adequate and the attack on the uterine musculature could hardly have been the exclusive result of an inadequate decidual reaction.

The possible inadequacy of the deciduum in the present instance is admitted, of course, as a likely maternal factor in the diffusion of the placenta (placenta diffusa); however, such a factor is believed to be subsidiary to the fetal factor described above.

Although the patient and child were lost in this instance, the authors do not regard the case, because of the poor published results of conservative methods of treatment, as an argument against the radical surgical approach to the problem.

The authors regret that the rarity of the condition and the difficulty or impossibility of making the diagnosis during the pregnancy has resulted in insufficient endocrinologic studies on these mothers to permit definitive conclusions with regard to the maternal hormonal factors in the pathogenesis of placenta accreta. JOHN W. BRENNAN, M.D.

Acute Surgical Emergencies of the Abdomen in Pregnancy. EDWARD HAMLIN, JR., MARSHALL K. BARTLETT, and JUDSON A. SMITH. *N. England J. M.*, 1951, 244: 128.

Any acute abdominal emergency occurring in the nonpregnant woman may occur during pregnancy. Early recognition of the existence of the acute emergency is of utmost importance. Persistent pain is the one early and almost invariable symptom of an acute abdominal condition. When the basic complication is promptly recognized and treated, there should be relatively little danger to the mother and to the infant.

From 1939 to 1948, there were 49 acute abdominal conditions among 26,341 women delivered at the Boston Lying-in Hospital. Ectopic pregnancies and traumatic ruptures of the uterus during delivery were excluded from this survey.

There was no patient with acute pancreatitis, or perforated gastric or duodenal ulcer. No case of incarcerated hernia was encountered, but 2 patients required inguinal herniorrhaphy because of pain.

Symptoms indicating gall-bladder disease were observed in 23 patients, but only 4 had definite acute cholecystitis. All of the patients recovered and went to term without surgical intervention. During pregnancy, the management of acute cholecystitis tended to be more conservative than it might have been in the nonpregnant woman, because of the increased technical difficulties of cholecystectomy in the presence of the large uterus and the possibility of miscarriage or premature labor due to the surgical trauma. However, failure of the acute symptoms to subside promptly under conservative treatment should be an indication for surgery.

The usual management of obstruction of the small bowel is not changed by the presence of pregnancy. Because of the frequency of vomiting during pregnancy, the clinical diagnosis is often difficult, as is also the x-ray interpretation of gas patterns because of the displacement of the intestines by the enlarged uterus. There were 3 patients with intestinal obstruction, all of whom had to be operated upon after decompression by intubation for various lengths of time had failed. In the first patient, a 25 year old para-i in the seventh month, there was a band obstruction in the midportion of the jejunum. Twelve hours after the operation she went into labor and delivered a 4 pound infant who survived. In the second patient, a 45 year old para-i at 5½ months, the obstruction was caused by a loop of small intestine adherent to a degenerated uterine fibroid. A small fetus, removed by hysterotomy, died after 2 hours. The third patient, a 34 year old para-i, had a myomectomy for a degenerating fibroid in the fourth month of pregnancy. Sixteen days later she had to be reoperated upon for intestinal obstruction because a loop of small bowel had become adherent to the myomectomy wound. One month later she expelled a macerated fetus. All 3 women recovered.

Appendicitis furnished the largest number of acute surgical emergencies. Because of the high maternal and fetal mortality associated with rupture of the appendix, all suspicious cases were explored. Thus, 22 patients were operated upon following a preoperative diagnosis of acute appendicitis, and in 6 of these (27.3%) the diagnosis proved to be erroneous. However, in none of the patients under observation did rupture of the appendix occur, and no miscarriage or premature labor followed any of the negative exploratory laparotomies. All 6 patients went to term and had uneventful deliveries.

Of the 16 patients in whom the diagnosis was correct, 12 had unruptured appendices which were removed without drainage. The period of gestation in these 12 patients ranged from 8 to 36 weeks and all had living infants.

Four patients admitted with ruptured appendices had symptoms from 4 to 14 days. Three had generalized peritonitis and 1 had a localized abscess. The appendical area was drained in all, the appendix being removed only in 1. All of the patients recovered and 3 of the infants survived.

Ovarian cysts discovered during pregnancy should be removed at once because of the impossibility of determining their exact nature by any other means, because of the danger of subsequent rupture or torsion, and because of possible obstruction of labor. If acute symptoms develop immediate intervention becomes necessary.

Eleven patients were operated upon for ovarian cysts, 2 as emergencies. Two patients with ovarian tumors diagnosed early in pregnancy were carried to term and delivered by section with coincident removal of the tumors by salpingo-oophorectomy. Upon 7 patients elective operations were performed at from 2 to 7 months of pregnancy. There was 1 stillbirth; 1 premature infant died, but there was no maternal death. Two patients did not return for delivery and the outcome is unknown.

Spontaneous rupture of the uterus is the most common surgical emergency involving the uterus itself. The diagnosis is obvious in the presence of pain, severe shock, and cessation of the fetal heart. However, the pain may be very slight or obscured by labor pains, and shock may be absent. The rupture may be entirely asymptomatic and unsuspected. Thus, it may be discovered during a repeated cesarean section, or it may be diagnosed after vaginal delivery when it is found that the placenta has escaped into the abdominal cavity, or several days later when peritonitis has developed. In all cases of suspected rupture, the uterus should be explored manually. The best treatment for rupture of the uterus is immediate supravaginal hysterectomy.

Spontaneous rupture of the uterus occurred in 9 patients. In 3 the rupture occurred at the site of a previous cesarean section. The 6 other patients were multiparas near term ranging from gravida-iii to gravida-ix, who had gone into labor. In 3 the rupture occurred after a few hours of labor, while in the 3 others it was discovered after vaginal delivery of living infants. One patient who sustained a cervical laceration, which was repaired, developed peritonitis and died; at autopsy it was discovered that she also had a rupture of the lower uterine segment.

Uterine fibroids occasionally show signs of degeneration, causing pain, tenderness, slight fever, and moderate leucocytosis which will usually subside with a few days of bedrest. Myomectomy during pregnancy should be done only if the symptoms are really severe and persistent, because of the possibility of miscarriage.

There were 6 patients with fibroids whose symptoms required operation. Myomectomy was performed in 5, and 4 of these had living infants at term. The fifth and sixth patients developed intestinal obstruction due to adhesions to the myomectomy wound and to a degenerated fibroid, respectively. These 2 patients recovered but the infants were lost.

There were 4 additional cases of uterine fibroids without acute symptoms in which operation was held advisable. In 1 patient a large pedunculated fibroid was removed; the second patient was explored because of the possibility of ovarian cyst, and a myomectomy was done; the third patient had a cervical fibroid which was removed vaginally; and the fourth patient was subjected to hysterectomy because of multiple fibroids. All of the patients recovered, and the first and third had living infants.

HERBERT TEICHNER, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

A Preliminary Report on Abdominal Aortography in Urology. I. H. GRIFFITHS. *Brit. J. Urol.*, 1950, 22: 281.

A small series of cases was presented in the hope of stimulating more interest in abdominal aortography. The author used an 18 steel-wire gauge needle which was inserted 4 fingerbreadths from the spinous processes at the level of the first lumbar vertebra. After the needle was felt to enter the aorta, 20 c.c. of 70 per cent diodone were injected in 5 seconds and 4 x-ray exposures were made at 2 second intervals as the last 10 c.c. were being expelled from the syringe.

It has been emphasized that diodone permits an immediate repeat performance if the first series of x-rays proves to be unsatisfactory. No toxicity to the drug was noted. It was inadvertently injected outside of the aorta in 2 cases with no ill effects and was completely absorbed within an hour.

The technique called for carefully co-ordinated team work. Aortography has not been advocated as a routine procedure but as a supplement to pyelography. It has been recommended especially when intravenous or retrograde pyelograms are inadequate, in retroperitoneal tumors of uncertain origin, and in cases of congenital anomaly of the kidneys, hematuria without pyelographic changes, unilateral hydronephrosis, peripheral vascular disease, hypertension, and aneurysm.

The author insists that the hazards are few and not serious.

ORMOND S. CULP, M.D.

Hydrocalycosis. THOMAS MOORE. *Brit. J. Urol.*, 1950, 22: 304.

After reviewing the normal anatomy of the calycine system, pathologic changes in hydrocalycosis are explained by alleged inability of one or more of the sphincters to function properly. The sphincter in the calyx just below the apex of the papilla has been designated "the sphincter of the calyceal fornix," that at the junction of the minor and major calyces has been called "the minor calyx sphincter," and that at the junction of the major calyx and the pelvis has been referred to as "the major calyx sphincter."

Four types of hydrocalyx are described diagrammatically and pyelographically: (1) fornical, (2) minor calyx, (3) major calyx, and (4) combined.

Cases reported by earlier writers have been interpreted on this basis and the terminology has been correlated with other popular terms that have been used to identify this type of lesion, e.g., pyelogenous cyst, calycine diverticulum, and intrarenal cyst.

The author believes that all of these sphincteric obstructions are due to achalasia, but admits that the cause of the latter remains unknown.

The disease may be symptomless or it may produce chronic renal pain. Superimposed infection, calculi, or both may alter the clinical picture. Hydrocalycosis can be diagnosed by intravenous and retrograde pyelography, but oblique and lateral views may be necessary in many cases.

Operative treatment usually is necessary although some hydrocalyces remain uncomplicated and require no treatment. A few cases are said to improve after dilatation of the site of the obstruction. The operation of choice includes obliteration of the calycine cavity. When the kidney has been replaced by cysts, nephrectomy will be necessary.

ORMOND S. CULP, M.D.

Nontraumatic Renointestinal Fistula (Le fistole reno-intestinali non traumatiche. GIOVANNI FORNI. *Arch. ital. chir.*, 1950, 73: 263.

Renointestinal fistula was recognized in remote times and was described by Hippocrates.

Fifty-seven cases of the nontraumatic type of renointestinal fistula, which have been reported in the literature, have been gathered together and minutely studied by the author.

Anatomically, the anterior surface of the right kidney in its upper and middle third is contiguous with the second portion of the duodenum, which descends far enough to lie across the right renal pelvis without the interposition of peritoneum, and in its lower third, it is contiguous with the posterior wall of the last portion of the ascending colon and the first portion of the transverse colon.

The anterior surface of the left kidney in its upper one-third is contiguous with the tail of the pancreas, while in its middle and lower thirds it is contiguous with the terminal portion of the transverse colon and the first portion of the descending colon.

The right renal pelvis is contiguous with the lower part of the second portion of the duodenum, while the left renal pelvis is contiguous with the posterior wall of the splenic flexure of the colon.

The pathological communication between the cavity of the kidney and the intestine is determined by the anatomical contiguity of the two organs.

From an etiological and pathogenic view point this affection manifests itself almost exclusively between the ages of 20 and 50 years with its greatest frequency between those of 25 and 35 years. It occurs slightly more frequently in females than in males.

The segments of the intestine are most often involved in the following order: colon, duodenum, sigmoid, and rectum.

The few cases in which the fistula involves a portion of the intestine not normally in contact with the kidney are explained by abnormalities due to the increase in size of the kidney, e.g., pyonephrosis,

and to acquired or congenital anatomical displacements, e.g., scoliosis, and visceroptosis with renal ptosis.

Pathologically, the prime cause of the formation of a nontraumatic renointestinal fistula is an inflammatory condition of the kidney. The renal symptoms, practically always, precede the intestinal symptoms. The renal affections follow an increasingly chronic course after a very brief acute phase with fever, renal colic, and diminution of diuresis. The intestinal symptoms indicate perforation which results from necrosis of the intestinal tissue contiguous to the inflamed renal tissues.

The most frequent pathological conditions which exist in the kidney are hydronephrosis, renal tuberculosis with mixed infection, and renal calculus with pyonephrosis.

The fistulas are correctly described as renoduodenal or renocolic, pyeloduodenal or pyelocolic, and pyeloureteroduodenal or pyeloureterocolic.

The symptoms of renointestinal fistula run a course, varying from 1 year to 35 years but usually from 1 to 8 years. The renal symptoms in cases due to hydronephrosis do not appear until the hydronephrosis reaches a noticeable size and is complicated by a superimposed infection. In cases due to renal calculi, there is a long history of periodic renal colic and later sepsis caused by superimposed infection and characterized by hematuria, albuminuria, and vesical pain.

When perforation occurs, the pyonephrotic sac opens into the intestine and a diminution in size of the renal tumefaction occurs. The urine is diminished in volume and takes on a fetid odor. Pneumaturia and biliuria occur.

The intestinal symptoms which occur are vomiting with characteristic urinary and ammoniacal odor, and diarrhea with urine, pus, blood, and at times renal calculi in the feces.

With the appearance of intestinal symptoms the renal symptoms diminish, the pain diminishes, and the renal tumor decreases in size.

After an acute stage, as described, a chronic stage of anorexia and general debilitation follow.

Fever is always present; it is usually mild except when an attack of renal colic occurs. Night sweats are common.

Renal pyelograms demonstrate the presence of a fistula.

Treatment of nontraumatic renointestinal fistula is surgical and consists of nephrectomy, excision of the fistulous tract, and closure of the intestinal orifice.

The mortality of the patients operated upon in this series was 25 per cent, (8 deaths in 32 cases). The mortality of the patients not operated upon was 60 per cent. BLACKWELL MARKHAM, M.D.

Hemangioma of the Kidney. ARTHUR J. BUTT and JOSEPH Q. PERRY. *J. Urol.*, Balt., 1951, 65: 15.

Historically, hemangioma of the kidney was first described by Virchow from an autopsy specimen, and first recognized clinically in 1903 by Fenwick. The congenital origin of the great majority of hemangiomas points strongly in favor of tissue predisposition as a prominent factor in their formation. Virchow believed that they were formed from imperfectly formed vessels. Rokitansky considered that angiomas represented simple hypertrophy of vascular segments without neoplastic growth. Thoma believed that much of the growth was due to mechanical factors.

Renal vascular tumors, both benign and malignant, may be of various sizes. They may vary from pin point size to massive forms. The tumors have a deep reddish color and may be located in the cortex, medulla, tip of a papilla, or subepithelially in the pelvis. They usually invade the surrounding kidney and are only occasionally encapsulated. Microscopically, they are blood-filled spaces lined with epithelium. The walls may be single layered or may contain layers of elastic tissue fibers.

The cardinal symptom is usually hematuria, which may persist for years. Operation may be necessary to control hemorrhage as a life-saving procedure. Pain is usually due to the passage of clots down the ureter. There are no characteristic findings. The patients are usually under 40 years of age. X-ray evidence may or may not be present. Treatment is usually surgical, and in most instances consists of nephrectomy.

A case is reported of a 60 year old woman with recurrent pain in the left flank and gross hematuria; the bleeding was worse after automobile rides and at the end of the day. Retrograde pyelograms showed a filling defect of the middle calyx of the left kidney. Six weeks later a repeat study showed the same findings. After preliminary transfusion, a nephrectomy was performed. Grossly, the kidney was normal. In the midportion there was a hemorrhagic tumor measuring 1.5 by 1 cm. which extended to the renal pelvis at the middle calyx. There were large and small blood spaces lined by a single layer of endothelium. There was a diffuse infiltration of the lymphocytic cells about certain of the cavernous spaces. Convalescence was uneventful.

The authors advise study of the urinary sediment for malignant cells in the differential diagnosis of urinary tract tumors. Conservative surgery in cases of benign renal vascular tumors is advised in view of the possibility of bilateral involvement.

NATHAN ROSENBLOOM, M.D.

Renal Angioma; Suspected Bilateral Involvement. BERNARD E. PALETZ and GEORGE SEWELL. *J. Urol.*, Balt., 1951, 65: 9.

The authors report a case of unilateral renal angioma with a strong suggestion of centralized involvement. The patient, a 21 year old negro, was admitted with complaints of profuse, gross, painless hematuria for 2 days. This was recurrent for the previous 10 years, and lasted from 1 to 7 days. One year before, he had had a "bladder tumor" removed transurethrally.

Cystoscopically, there were spurts of blood from the right orifice but none from the left one. Indigo carmine appeared normally, bilaterally. Pyelograms were normal on the left side but showed dilatation and some irregularity of the superior calyx on the right. No acid-fast organisms were found on repeated stains. Because of persistent hematuria 3 transfusions were given. A preoperative diagnosis of hemangioma of the right kidney was made and nephrectomy advised as a life-saving measure. Surgery was uneventful.

Grossly, the specimen was not remarkable except for tiny scattered spots throughout the medulla. Microscopically, scattered throughout the medulla there were numerous dilated vascular spaces filled with fresh blood. They varied in size from 25 to 300 mμ. In areas there was a definite cavernous pattern. Nowhere was there proliferation of the endothelial cells suggestive of hemangioendothelioma. The diagnosis was multiple, diffuse hemangioma of the right kidney.

Six weeks later the patient returned with gross hematuria which had started 3 days after he left the hospital. Three weeks later there was a recurrence of the hematuria with practically pure blood spurting from the left ureteral orifice. Because of alarming hematuria, 7 transfusions of 500 c.c. each were given. It was suspected that the same type of pathology existed in the remaining kidney. At the advice of the roentgenologists, radiation of the left kidney was done. An anterior and a posterior port were used with 200 roentgens in air per field per day on each of 2 consecutive days. The total estimated dose to the kidney was 435 roentgens. The roentgenologist estimated that it would take 6 weeks for any effect. The kidney pelvis was irrigated with 1:1,000 silver nitrate solution, but the bleeding persisted. Approximately 5 weeks after irradiation the bleeding ceased very suddenly; the urine remained clear on follow-up examination to the present date.

The authors advise nephrectomy for renal hemangiomas. Exploration alone for hematuria might not reveal small lesions or diffusely scattered lesions, as in this case. In bilateral cases, irradiation is suggested. NATHAN ROSENBLOOM, M.D.

Mesonephroma of the Renal Pelvis (Sul mesonefroma della pelvi renale). S. SERRANO. *Arch. ital. urol.*, 1950, 24: 197.

A 65 year old woman began to suffer 10 years previously from intermittent attacks of pain in the right half of the abdomen accompanied by mild elevations of temperature and some urinary turbidity and discharge of mucus and pus. Five months previously the attacks became more severe and since then the pain and some temperature had persisted. At this time the kidney on the right side was found, on palpation, to be larger than normal. One month previously, during an especially severe attack of pain, some blood and fragments of tissue were passed. Histologic examination of this tissue was positive for neoplasm.

Following nephrectomy, the drainage canal failed to heal, tumor tissue and blood were expelled intermittently, cachexia appeared, and death occurred 2 months after the operation. Autopsy was refused.

The removed kidney was not greatly deformed; however, it was thicker (7 cm.) than normal (3 cm.) and this increase in size was especially pronounced in the lower region and toward the hilus, so that there was a protrusion into the lower half of the concavity of the hilus. This protrusion consisted of a walnut-sized mass which had pushed backward and deformed the pelvis and stump of the ureter. Over this region the kidney itself gave an impression of increased consistency and the capsule was somewhat thickened and adherent; the kidney substance beneath the capsule presented tiny cysts filled with a limpid fluid.

On cross section the pelvis was found to be greatly enlarged and occupied by a fungous, grayish tissue, which was soft, rather friable, and exhibited abundant areas of a dark-reddish color due to sanguineous extravasations. This mass rather regularly followed the dilated and deformed calyces and in places had infiltrated into the parenchyma of the renal medulla. The pyramids were being destroyed, either by pressure or by infiltrative invasion. On the whole, the parenchyma surrounding the neoplasm seemed reduced in amount and of increased consistency.

Histologically, the neoplasm presented a rather disconcerting appearance from the standpoint of classification. The growth, as a fact, presented two fundamentally different aspects; there were areas which were of carcinomatous appearance and others of an endotheliomatous reticulosarcomatous aspect.

The tumor itself was constituted essentially of papilliferous tissues, the papilli being covered with a polystratified epithelium which proffered an epidermoidal aspect on the surface; many of the papilli, with regard to the nucleoprotoplasmic relationship, were regarded as atypical cells. In places in the tumor depths these cells tended to run together into epidermoidal pegs, rods, and irregular masses which frequently assumed a giant cell-like mass, with as many as 20 centrally located nuclei; this, the author assumed, represented a tendency toward syncytial formation.

Beneath this epidermoidal component the tumor cells tended toward a fusiform shape and emitted fine prolongations which united with prolongations of the neighboring cells, and thus a sort of rete of highly atypical cells was produced. Here there were giant cells with bicyclic huge nuclei or nuclei which were broken up and stained deeply with hematoxylin. The appearance was in fact that of a sarcoma.

Still more deeply in the tumor tissue there appeared more and more the characteristics of a mesenchymal neoplasm; the cells here were separated by a reticulum which stained blue with the Mallory test and became impregnated with silver by the

reaction of Rio-Hortega. These cells were arranged around the blood vessels in places and in other places formed the sole lining of the vessel; in some places an endothelial lining could be recognized and in others not.

A singular phenomenon of this tumor was the presence among the large, neoplastic cells of a yellowish, amorphous substance, staining rose-colored with eosin and the Van Gieson stain, and azure blue with the Mallory stain, and which formed masses of hyalin or a rete of coarse fibers within the cells themselves.

In this deepest region there were also cavities lined with cubical cells, reproducing in substance the aspects which have been reported as peculiar to the lymphangioendothelioma or to carcinoma of the peritoneum. Here there were also villous formations covered with flat epithelium, an epithelium which was stratified and hyperplastic. Where the covering was lacking the exposed tissue presented a reticulosarcomatous structure which could almost be designated by the term fibroepithelioma.

Thus, it was evident that this was a reticulosarcoma with endotheliomatous aspects, a renal papilloma with sarcomatous degeneration of the stroma, a carcinosarcoma, or, in general, a mixed tumor of the kidney. The author accepted the diagnosis of mesonephroma, according to the classification of Culp and Hartman (*J. Urol.*, 1948, 60: 552); that is, he believed it to be a mixed carcinosarcomatous tumor with lymphangio-perithelio-reticulosarcoma-polymorphocellular components.

This type of tumor has nearly always been found situated deeply within the parenchyma of the kidney, and its involvement, in this instance, of the renal pelvis is a great rarity. The explanation of its presence at this location may perhaps be ascribed to the chronic irritation by the urinary infection as manifested by the preceding 10 years of urinary symptoms. JOHN W. BRENNAN, M.D.

Discussion on Partial Nephrectomy. HOWARD G. HANLEY, E. W. RICHES, ARTHUR JACOBS, H. HAMILTON STEWART, and OTHERS. *Proc. R. Soc. M.*, Lond., 1950, 43: 1027.

H. G. HANLEY reported the results of partial nephrectomy performed by various surgeons in 155 cases. He differentiated heminephrectomy from partial nephrectomy. Heminephrectomy is the removal of half of a double kidney. It is often performed for hydronephrosis, ectopic ureteral opening, or calculi. Partial nephrectomy, on the other hand, is the removal of portions of the kidney parenchyma. In the cases studied, partial nephrectomy was performed 125 times for stone; hydrocalycosis, solitary cysts, tuberculosis, neoplasm, and hydronephrosis were the other conditions treated by partial nephrectomy.

Among the indications for partial nephrectomy, the most common was a fragmented, irregular stone of low roentgenologic density, fitting the calyx snugly. The stone was located in the lower calyx in 83 of the 125 calculous cases. In 12 of these a bilateral partial nephrectomy was done. The removal of the diseased calyx and its lining membrane in these cases was believed to have been of value in reducing recurrences. The exact recurrence rates are not available, but in this series the rate seemed to be at least 11 per cent.

The author states that in certain instances partial nephrectomy may be useful in the treatment of tumors and tuberculosis of the kidney. In the latter disease, the localized ulcerating lesion seems best suited for surgical resection.

In discussing the technique of the operation, Hanley stated that he favored maintaining hemostasis by manual pressure on the renal pedicle. After the blood supply to the kidney is closed off, the author removes a wedge of kidney with the scalpel rather than by diathermy. No attempt is made to stop the bleeding except by placing a piece of fat in the defect. The capsule is closed without tension over the plug of fat. In general, the author does not use a drain in these cases.

Secondary hemorrhage and urinary fistulas are the main complications of this procedure. Both can usually be treated adequately without further surgical intervention. In this series there was only 1 operative death.

E. W. RICHES discussed his preference for the term "calyceal diverticulum" rather than hydrocalycosis. He thought it best to close the neck of the calyx with a fine suture if this were possible.

H. H. STEWART suggested the removal of a calyx which could be incriminated as the site of the stone's formation even though the stone had been dislodged and was located in the pelvis or ureter at the time the patient was first seen by the physician. He cited instances in which he had followed this line of reasoning. JOHN T. GRAYHACK, M.D.

Tumors of the Vesical End of the Ureter. F. MASINA. *Brit. J. Urol.*, 1950, 22: 320.

Forty cases of tumor of the lower end of the ureter were found among 800 patients with neoplasms in the urinary tract. Some of these were associated with tumors of the kidney. Others occurred in conjunction with carcinoma of the bladder. This is primarily a pathologic study of the tumors in this area, with no attempt to discuss late results of treatment.

For descriptive purposes the vesical end of the ureter was divided into three parts, the juxtavesical, intramural, and submucous portions. The tumors presented themselves in a variety of ways, forming slight elevations of the intravesical portion of the ureters or submucous hillocks resembling ureteroceles.

Attention was directed to the fact that such lesions may be overlooked and therefore require careful coordination of all conventional diagnostic methods. The author has been especially impressed by the value of intravenous pyelography and bimanual examination of the empty bladder under anesthesia.

Conservative treatment by endoscopic resection or fulguration after ureteral meatotomy was favored as long as the pyelograms and bimanual examinations remained normal.

When tumors became palpable or the pyelogram showed stasis, open surgery was preferred. Nephroureterectomy is recommended for low grade malignancies, but when the tumor proves to be infiltrating, simultaneous partial cystectomy is urged. In some instances, total cystectomy was considered necessary. ORMOND S. CULP, M.D.

Our Experience with Ureterosigmoidostomy (La nostra experienza nell'ureterosigmoidostomia). G. MAZZOTTI. *Urologia*, Treviso, 1950, 17: 401.

A hundred ureterosigmoidostomies were done on 58 patients during the past several years. This material included 7 cases of exstrophy of the bladder with 2 deaths (28.5 per cent), 2 cases of severe epispadias without mortality, 10 cases of otherwise uncorrectable vesicovaginal fistula with 3 deaths (10 per cent), 34 cases of tumor of the urinary bladder with 9 deaths (30 per cent), 2 cases of tuberculous cystitis without mortality, and 1 case each of vesical (Hunner's) ulcer, diverticulosis, and trauma, all without mortality. This amounts to a total mortality of 24.1 per cent.

Coffey's first method, with slight modifications, was employed almost exclusively. The transverse incision in the seromuscular wall of the sigmoid colon was used (method of Davalos) instead of the original longitudinal incision. The ureters were led to the area of implantation subserously: a curved forceps was introduced through the peritoneum of the sigmoid mesocolon, immediately adjacent to the point of implantation, and a canal was burrowed to the upper point of the isolated portion of the ureter. This was done to produce a single tract, for more than one tract was created by intermediate opening of the covering peritoneum. This subserous placing of the transposed ureteral section has the advantages of shortening the time for burying the ureter beneath the peritoneum, of avoiding the possibility of pocket formation and subsequent hernial incarceration, of nutritional advantage to the transposed organ through the closer relationship with the vascular subserous tissues, of a more natural direction, and of greater liberty of motion in the loose-meshed retroperitoneal tissues.

No special area for implantation was insisted upon, the area being selected in conformity with the conditions encountered in the individual case. The incision in the seromuscular coat of the wall of the sigmoid is not directly transverse but is more of a swallow tail (like an inverted Y); this is intended to forestall a subsequent choking off of the ureteral lumen at this point. The course of the incision through the sigmoid wall is not a long one, but is more sharply oblique. The stump of the ureter is coaxed through the incision along the groove of a hollow director and is brought out into the cavity of the sigmoid colon and fixed to its inner (mucous) surface with the aid of a fine silk suture traversing the apex of the obliquely trimmed ureteral termination and brought out through the wall of the gut, about 0.5 cm. distal to the inner opening of the incision, by means of a needle on each end of the thread. This stitch and a U-suture at each side externally, barely involving the muscular layer of the ureter, are tied and thus anchor the implant securely in place. The whole is then usually buried by a single Lembert suture and the spot snugly covered by the neighboring serous structures (usually the appendices epiploicae). Special emphasis is placed on the use of large guy sutures in the closure, embracing the full thickness of the abdominal wall and taking the stress from the approximating suture in the layers.

The antibiotics and the sulfonamides are, of course, used both prophylactically and to combat postoperative infections. When vomiting is controllable, streptomycin is preferred to chloromycetin. A few injections of vitamin B_6 are indicated as a rule. Aside from the febrile reactions, which at present are usually mild and easily controlled, the chief difficulty lies in preventing a necrosis of the ureteral stump and the formation of a valve effect with consequent dilatation of the ureter. However, this latter complication is not very troublesome with the author's present technique of operation; it is an early manifestation and disappears rapidly as a rule. In 1 instance the roentgenogram caught a typical pneumoureter, the collection of gas in the ureteropyelic lumen probably being due to some sort of valve effect. Such a possibility contraindicates lengthy implantation trajectories through the wall of the sigmoid.

Modern prophylactic and postoperative techniques (antibiotics) have greatly extended the indications for this operation, but, of course, such assistance cannot replace early diagnosis and speedy correction of the postoperative emergency.

JOHN W. BRENNAN, M.D.

BLADDER, URETHRA, AND PENIS

Vesical Tumors; An Analysis of a Personal Series. DAVID BAND. *Brit. J. Urol.*, 1950, 22: 381.

The author has analyzed 176 of his 200 cases of vesical tumors, 64 per cent of which were in the male, and the largest number occurring in the seventh decade. Papillomas accounted for 53 per cent of these tumors, and 47 per cent were carcinomas. Four of the proved papillomas developed carcinoma from 8 months to 10 years following treatment. The proportion of single to multiple papillomas was 3 to 1, and in 5 cases multiple malignant tumors were noted. The most frequent site of the tumor was on the lateral walls of the bladder, and tumors on the posterior wall and base and neck of the bladder were one-third as common. The cystoscopic diagnoses agreed with the pathological sections in all but 1 case.

Transurethral fulguration was performed in 57 cases and is the treatment of choice when adequate follow-up can be made. This treatment was unsatis-

factory in 3 cases because of frequent recurrences. Transurethral resection was performed in 6 cases and is considered the treatment of choice when the tumor is near the bladder neck. Diathermy and open operation was performed in 20 cases; in 2 of these metastases occurred in the suprapubic scar. Partial cystectomy is the treatment of choice in these cases. Three patients were treated by open operation and irradiation; this was done when the diagnosis was in doubt or a very extensive and apparently simple tumor was present. Undesirable reactions followed the use of radium, such as tissue necrosis and sepsis. Deep x-ray therapy was performed in 3 cases because of an extensive tumor or minute multiple papillomas or tumors of the vault in which cases partial cystectomy is contraindicated. Total cystectomy is preferred if hemorrhage has been severe, and was performed in 2 cases.

HERBERT J. KAROL, M.D.

The Results of Diathermy Treatment of Villous Papilloma of the Bladder. F. G. HOLLANDS. *Brit. J. Urol.*, 1950, 22: 342.

The author reports his conclusions after studying the course of 408 villous tumors of the bladder treated by diathermy at the Birmingham United Hospitals between 1920 and 1944. A villous papilloma is taken to be a pedicled or sessile fronded tumor, single or multiple, which may be histologically benign or of doubtful, low, or medium malignancy. The results reported are based on a minimum cystoscopic follow-up of 5 years.

The diversity of behavior of the villous papilloma makes its course completely unpredictable in any given instance. However, the cases seem to fall into the following general groups on the basis of their behavior after initial treatment: (1) cases in which no fresh growth occurs; (2) cases with low tendency (one or two tumors over several years) to new growth occurrence; (3) cases with a medium tendency (less than 15 per year) to new growth occurrence; (4) cases with high rates of recurrence, approximating localized or generalized papillomatosis. Occasionally a case classified in one group may by subsequent activity be necessarily changed to another.

In evaluating the results of therapy, local recurrences, failure to prevent the normal evolution of the disease, and recurrences at special sites, such as the internal urinary meatus or cystotomy wound, were considered evidences of failure. Cases developing only sporadic recurrences were considered as successes.

Perurethral diathermy was used in the treatment of 184 patients with villous growth. One hundred were treated as anesthetized in-patients. Sixty-two of these were considered successfully treated. Eighty-four patients were treated as unanesthetized out-patients. Treatment was successful in only 40.5 per cent of these. In studying the cause for failure it seemed that as far as local recurrences were concerned, the size of the tumor had little to do with its response. However, the more sessile tumors, grossly, and the more malignant tumors, histologically, seemed more likely to recur at the site of attempted therapy. In addition to the nature of the tumor, the local recurrence rate seemed to be influenced by the thoroughness of treatment. The cases in which several attempts were necessary initially to apparently eradicate the growth had a higher recurrence rate than those in which the first treatment seemed to eliminate it.

In addition to success in controlling single growths, treatment by perurethral diathermy was satisfactory in about two-thirds of the patients who showed a marked tendency to develop new tumors. The author believes that multiple growths warrant a trial treatment with diathermy. In deciding when to abandon this therapy for more radical measures, he uses changes in histological appearance of the tumors and an excessively high rate of new growth formation as criteria.

An increase was noted in the occurrence of tumors at the internal urinary meatus and in the posterior urethra after both perurethral and suprapubic treatment. Many of these could be subsequently treated satisfactorily by diathermy.

In addition to the tumors treated perurethrally, 224 cases of villous papilloma were subjected to open diathermy. Of these, 48.9 per cent were considered to have been successfully dealt with. The failures in this group included a 10 per cent recurrence rate in the cystotomy wound. No further discussion of failures in this group was given.

JOHN T. GRAYHACK, M.D.

A Pull-Through Operation for Impassable Traumatic Stricture of the Urethra. A. W. BADENOCH. *Brit. J. Urol.*, 1950, 22: 404.

The operation to be described has been performed seven times on 5 patients with impassable stricture of the urethra, with moderate success.

A suprapubic cystotomy is first performed and a metal sound is passed from the external meatus to the point of stricture. An incision is then made at the perineal scrotal junction and the ischiocavernosus muscle is split. The urethra is exposed and divided just distal to the stricture, which is usually at the inferior layer of the triangular ligament. The distal urethra is then mobilized for 4 to 6 cm. With another sound inserted in a retrograde manner to the proximal end of the stricture, the scar tissue is incised and the sound is forced through to produce an artificial tract which is adequately dilated. The tip of the retrograde sound is invaginated into the open end of a catheter which has been passed into the proximal end of the distal section of the urethra and sutured. The catheter with the mobilized section of urethra attached is pulled through the artificial opening in the triangular ligament into the bladder and the cut end of the bulb enters the prostatic urethra. The cystotomy is closed about a self-retaining catheter and the perineum is closed in layers. About the seventh day, the urethral catheter extending out through the suprapubic wound sepa-

rates. Dilatations at progressive intervals are begun about the fourteenth day.

This operation is suited particularly to those cases in which the stricture cannot be excised, or, after excision, the ends cannot be approximated by the methods of Marion or Hamilton Russell.

HERBERT J. KAROL, M.D.

GENITAL ORGANS

Results of Suprapubic Prostatectomy (Ueber die Ergebnisse der suprapubischen Prostatektomie). F. GAERTNER. *Zschr. Urol.*, 1950, 43: 443.

For the purpose of comparing the results that can be obtained by use of the ordinary suprapubic (Freyer) prostatectomy, supplemented by the Harris-Hryntschak method of suture of the prostatic bed, with those universally claimed for the newer retropubic (Millin) method, which has several objections, the author presents a report of 482 prostatectomies performed at the First Surgical University Clinic, in Vienna, during the 4 year period from 1944 to 1947. Fifty per cent of these patients were admitted to the Clinic because of repeated attacks of urinary retention; none of them was able to urinate spontaneously. Of the remaining 50 per cent of patients, 40 suffered from frequency of urination, severe nocturia, infected urine, and vesical tenesmus. In this group the residual urine always amounted to more than 100 c.cm. The remaining 10 per cent of patients were suffering from prostatic hematuria; in 6 of these the condition was so severe that the patient had to be operated upon as an emergency measure.

There were 30 deaths; the remaining 452 patients who had been operated upon were discharged as cured. In 50 per cent of the total number, healing was without complication, the wound healing by primary intention without penicillin; the stitches were removed on the sixth postoperative day and the indwelling catheter was removed on the ninth or tenth day. After removal of the catheter the patients were always able to urinate spontaneously.

During 1949 prophylactic penicillin in a total dosage of one million Oxford units were given and penicillin was administered following the operation. This medicament seemed to result in earlier healing, and in an increased number of wound closures by primary intention; nevertheless the indwelling catheter was always left in place for at least 8 days. However, the total amount of time in the hospital has been reduced to 14 days, which compares favorably with the hospital stay after the Millin procedure. More important than reducing the postoperative hospital internment is a lengthening of the preparatory hospital period, since the preoperative indwelling catheter frequently results in an astonishing improvement in functioning of the kidney.

Of the 50 per cent of patients in whom healing occurred with some form of complication, 15 per cent suffered a short period of urinary incontinence; 12 per cent were detained in the hospital because of healing by second intention, or by a sort of pulmonary complication as a result of thrombosis; 5 per cent of the total number suffered postoperative bleeding. Seventeen patients suffered an epididymitis, many of these in spite of the fact that the vas had been partially excised. In 4 patients paraurethral abscess developed as a result of a decubitus from the indwelling catheter, and in one of these the urethral fistula is still present. Eleven patients were detained in the hospital because of a stubborn cystitis as a result of suppuration of the prostatic bed. In 1 patient an abscess at the point of ligation of the vas had to be incised.

The follow-up material, after exclusion of those patients dying in the hospital, consists of 452 cases. Of these, 329 were heard from. Thirty of this group had died; however, more than 20 of these deaths were certainly not connected with the operation itself. Only 2 could be counted as a result of the operation, and 1 of these was of a patient with carcinoma.

Thus, 259 of patients who could be followed up were totally free of symptoms, could retain the urine for periods of 4 to 10 hours, and were free of nocturia. All had put on weight and were able to resume their previous occupations.

Of the follow-up material, 32 patients still complained of some urinary abnormality; 15 showed a cloudy urine which, in most cases, was easily controlled by urinary disinfectants and galenicals. In 2, the condition occurred as the result of small bladder diverticula; 2 patients had easily dilated structures; 3 had urinary stones, and 2 had cystitis resulting from vesical papillomas.

Most remarkable, however, were the reports on the sexual function. Of these patients, 182 were able to perform the sexual act; 82 did not notice any difference in the sexual act from their previous capacity. All these patients felt themselves to be potent, and many professed an increased libido. Even those with vas ligation could ejaculate. A hundred of these patients could perform the act but did not note any emission of semen; many of these, however, were found to ejaculate backwards into the bladder. The fact that a greater number of those operated upon earlier could ejaculate normally is ascribed to the fact that the internal sphincter had regained its function. JOHN W. BRENNAN, M.D.

Early Correction of Congenital Chordee and Hypospadias. ORMOND S. CULP. *J. Urol.*, Balt., 1951, 65: 264.

A plea is made for the early correction of severe chordee and hypospadias before children start to school. While other types of surgical repair have been followed by an alarming and discouraging incidence of complications, the three stage Cecil operation has produced consistently excellent results without fistulas or other disagreeable features. A slight modification of this procedure was used to correct 24 chordees and to construct 19 new urethras.

The first stage or straightening operation was performed preferably during the first 2 years of life.

If the patient had not been circumcised, simple redeployment of the hooded prepuce provided sufficient skin and made more complicated operations unnecessary. Adequate straightening is urged before any attempt is made to construct an additional part of the urethra. Occasionally the first stage had to be repeated, especially in older patients. After satisfactory straightening, the urethral meatus usually was displaced to a position near the penoscrotal junction.

At 4 or 5 years of age, or 2 to 6 months after the first operation in older boys, the second stage or urethral construction operation was done over a splinting urethral catheter by the Thiersch-Duplay method. The new urethra was buried in the scrotum to avoid fistulas. In a few patients urine leaked from the incision after removal of the catheter, but all the wounds healed spontaneously.

The penis and urethra were freed from the scrotum at a third stage operation, which was feasible after 2 months had elapsed. Longer delays produced no hazard.

The technique of the three stage operation is given in detail with illustrating photographs. Five of the 19 patients had undergone from 2 to 9 previous unsuccessful urethroplasties. Ten of the 19 were cured by the time they were 6 years of age.

ORMOND S. CULP, M.D.

MISCELLANEOUS

Renal Tract Delay Time and Dead Space. R. R. MCSWINEY and H. E. DE WARDENER. *Lancet*, Lond., 1950, 259: 845.

The authors have made observations on the time necessary for the urine, after formation, to traverse the renal collecting tubules, calyces, pelvis, ureter, bladder, and urethral catheter; the volume of all these structures together is referred to as the "renal tract dead space," and the time needed for the urine to traverse them may be called "renal tract delay time."

Previous work on this subject has been scanty and although the problem has been recognized, few data are available. The authors' observations depend on the principle that if the dead space is x ml. and the urine flows at v ml. a minute, the delay time is x/v. Since urine flow is easily measured, if either the delay time or the dead space is known, the other can be calculated.

Twenty-four observations were made on 17 persons with a multi-eyed catheter. After the spontaneous flow of urine was made, sodium p-aminohippurate was injected intravenously and the urine collected; it was tested for P.A.H. by the Bratton and Marshall method. It was noted that a clear end-point was not seen and that there was an increase in concentration in several samples; thus, as expected, considerable mixing took place in the dead space and made an accurate estimation of it impossible. The delay time was again tested in 9 persons given large amounts of water; in these a high stable flow of urine was reached.

It was seen that with the urine flow above 2 ml. per minute the method was more accurate and the total P.A.H. delay time in 14 people was between 1.5 and 3.1 minutes, with an average of 2.4 minutes; the corresponding dead space was between 5.4 and 30.7 ml. The methylene blue technique gave a delay time of 1.5 to 217 minutes with an average of 2.2 minutes. This unexpected constancy in delay time at rates of urine flow between 2 and 14 ml. per minute implies that the renal tract dead space is capable of expanding from 5.4 to 30.7 ml. The site of this increased capacity of the renal tract at high rates of urine flow is a matter of speculation. It is implied by the authors that the bladder dead space approximated zero and that the renal pelves, the tubules, or both were the site of the renal tract expansion.

NATHAN ROSENBLOOM, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Occurrence of "Juvenile Bone Cysts" in a Family (Das familiaere Auftreten von "jugendlichen Knochencysten"). HELMUTH GIESEKING. *Chirurg*, 1950, 21: 670.

The author reports the case of a family in which 2 children had bone cysts of the humerus and femur, respectively, whereas the third child suffered a fracture of the humerus from a minor injury. The author assumes that in this last case an early stage of cyst was present which could not be visualized roentgenographically, but which was responsible for the fracture.

The theories of pathogenesis of bone cysts, their relation to giant cell tumors, to osteogenesis imperfecta, and to constitutional inferiority of the skeletal system are discussed briefly.

WERNER M. SOLMITZ, M.D.

Juvenile Bone Cyst and Accident (Jugendliche Knochencyste und Unfall). MAX LASTHAUS. *Chirurg*, 1950, 21: 672.

The question whether juvenile bone cysts can be caused by accident is not only of theoretic interest, but is of practical importance. Insurance claims are frequently based on the assumption that bone cysts, having caused pathologic fractures or other disturbances, have been produced by an injury.

The author discusses briefly the gross and histologic anatomy and the differential diagnosis of bone cysts, and reviews the various theories concerning their pathogenesis, which have been proposed during the last few decades.

The cysts occur most frequently between the sixth and the twentieth year. The site of predilection are the proximal epiphyses of the long bones. These cysts are filled with serous or bloody fluid, in rarer instances with proliferating fibrous tissue; they may be unilocular or multilocular. Histologically, the wall of the cyst contains fibroid, osteoid, or osseous tissue. Giant cells are frequently present. The cysts seem closely related to giant cell tumors and bone fibromas.

The diagnosis is usually made by radiologic examination; however, in most cases it is impossible to differentiate, in the x-ray picture, bone cysts from other lesions such as fibroma, giant cell tumor, myxoma, chondroma, or Brodie's abscess. In addition, osteitis fibrosa, echinococcus, tumor metastases, and other disturbances have to be ruled out.

Many writers believe that bone cysts could be caused by injury. The author rejects this theory, and it is his belief that the juvenile bone cyst is a localized benign tumor, originating from displaced mesenchymatic tissue. He states that there is no relation between Recklinghausen's disease and bone cysts. In the author's experience with 26 bone cysts and 15 giant cell tumors, no connection between an accident and the development of the cyst could be found.

WERNER M. SOLMITZ, M.D.

The Natural Course of Osteoid Osteoma. ERIK MOBERG. *J. Bone Surg.*, 1951, 33-A: 166.

The true nature and cause as well as the natural course of osteoid osteoma are unknown. Two case histories are presented. The first case was that of a man aged 23 years, with a lesion localized in the upper right thigh. X-ray examinations were performed three times during a period of 8 months and revealed development of the process as presented in three serial figures. The diagnosis in this case was verified histologically.

In the second case, a woman aged 24 years complained for more than 2 years of increasing symptoms in her foot. Two roentgenograms were made 16 months apart. Progression of the process was confirmed. An operation was performed and the diagnosis was verified histologically.

The literature on this subject is discussed. It is assumed that the disease has a natural healing process. These cases, which were verified histologically, showed that in the development of the disease process the small central nidus may increase through further destruction until it becomes larger than the cross section of the normal skeleton at a given point. Two clinically and roentgenographically typical, but histologically unverified cases gave grounds for the conclusion that the natural course leads to spontaneous healing.

RICHARD J. BENNETT, JR., M.D.

Osteoid Osteoma; A Clinicopathologic Study of 20 Cases. MALCOLM B. DOCKERTY, RALPH K. GHORMLEY, and ALFRED E. JACKSON. *Ann. Surg.*, 1951, 133: 77.

In 1935 Jaffe described, under the title of "osteoid osteoma," a peculiar lesion of bone which previously had not been recognized as a distinct entity. Clinically the lesions behaved like atypical osteomyelitis, and roentgenologically they exhibited many of the features of sclerosing osteomyelitis of Garré. Microscopically the lesions lacked the features of inflammation and presented instead many of the elements of a benign neoplastic condition. Typically there was a soft, brownish, ridiculously small, centrally located nidus consisting of osteoblasts and osteoid tissue in a fibrovascular matrix, and about this there was usually a disproportionately extensive zone of osteosclerotic bone. Two questions arose: (1) Is osteoid osteoma an entity? (2) Is the lesion inflammatory, degenerative or neoplastic? The first of these has been settled by an affirmative answer. The latter remains to be proved conclusively; however, the majority of the authorities side with Jaffe and Lichtenstein, and classify the condition as a type of osteoma.

In order to obtain material for their study, records of cases bearing the diagnosis "sclerosing osteitis," "Brodie's abscess," "solitary cortical abscess," "localized osteitis fibrosa," "osteofibroma," "osteoma," and "osteoid osteoma" were drawn from the files of the Mayo Clinic by the authors. As a preliminary they excluded all cases in which frank pus was encountered at the time of operation, those in which large sequestra were present, those in which multiple bony defects were found and, finally, all cases in which microscopic material was not available for study.

This screening process left about 150 cases for further analysis. The surgical specimens available in each instance were secured and reviewed. Notes were made on the weight of tissue removed and the general characteristics. Careful search was made for soft tissue fragments which might represent the nidi of osteoid osteoma. An average of six blocks was selected from each specimen and these were placed in decalcifying solution preparatory to sectioning which was done both by the freezing and the paraffin methods. Staining with hematoxylin and eosin was employed routinely. Roentgenograms, when available, were secured and scrutinized for radiolucent and radiosclerotic areas. An attempt was made to make a diagnosis from the roentgenogram in each case in an effort to evaluate the importance of this method as a single diagnostic test for osteoid osteoma. A review and summary of the clinical symptoms and signs were next made objectively in an effort to evaluate the importance of the clinical study in the diagnosis. In the resulting 48 cases the typical clinical and roentgenographic features of osteoid osteoma were present. In 20 of these, microscopic examination of tissue confirmed the diagnosis.

All evidence points to the fact that surgical excision is the treatment of choice and that excellent results are obtained from surgical excision provided that the nidus is removed at the time of operation. Whether spontaneous healing or regression of this lesion may occur seems to be a problem which can hardly be solved in the light of present knowledge. Because of the fact that the diagnosis can be made only by microscopic examination of the tissue and the discovery of a typical nidus, it would seem that if spontaneous healing occurred in any case, a diagnosis of osteoid osteoma could never be made unless this occurs in a recurrent lesion in which the diagnosis has definitely been established.

In an article by Brown and Ghormley, it was implied that the lesion of osteoid osteoma did not exist. The authors are glad to be able to correct this viewpoint and add their support to the large group of investigators who have recognized the lesion and reported on it in the literature. They are, however, as yet unable to prove whether the lesion is inflammatory or neoplastic. A recent review of all of the cases in the group which Ghormley previously reported as "solitary cortical abscesses" revealed that from the standpoint of history, clinical findings, and roentgenograms, these cases could not be distinguished from the authors' cases of osteoid osteoma. Ten of the patients in that group were not operated on; therefore no tissue examination was made. It is possible of course that some, or even all, of the patients who were not operated on actually may have had osteoid osteomas. The pathologic findings in those cases in which operation made tissue available indicate that they were not cases of osteoid osteoma.

Are osteoid osteomas and solitary cortical abscesses then two phases of an essentially similar process? Are they variants of a single process, or actually two different lesions with similar clinical and roentgenographic pictures? In one instance an atypical picture of osteoid osteoma has developed in what seemed to be an osteoid osteoma from the clinical, roentgenographic, and pathologic picture. This is the only case in which the authors felt they might say that a true neoplastic type of change had been observed. On the other hand, they know of one case in which they observed the clinical and roentgenologic characteristics of osteoid osteoma several years ago, but operation was not performed and therefore the diagnosis was never proved. Recent follow-up reports in this case, together with roentgenograms, indicate that the lesion has disappeared. Such observations lead them to believe that this type of lesion may at times develop one type of pathologic picture and at other times a different picture.

The Pathology of Calcareous Tendinitis and Subdeltoid Bursitis. HERBERT E. PEDERSEN and J. ALBERT KEY. *Arch. Surg.*, 1951, 62: 50.

A consideration was made of the gross and microscopic appearance of the lesion found in the rotator cuff of the shoulder in the condition termed "subdeltoid bursitis with calcification." A brief description was also given of the changes which occurred in the walls of the bursa.

A study of the material removed from the shoulders of 55 patients suffering from subdeltoid bursitis with calcification indicates that the basic process is degeneration of tendon or muscle in the rotator cuff of the shoulder.

It appears that the calcium is deposited in the necrotic collagenic tissue either with or without loss of its fibrous structure.

The necrotic calcified material may become enclosed in a granuloma wall, and when the collections of the material are large enough and sufficiently impregnated with calcium, they become visible in roentgenograms.

While inflammation with its tissue tension may produce some pain, another cause of pain is mechanical, dependent on tension within the granuloma.

Since the major cause of pain is the larger, calcified necrotic focus which is usually demonstrable on roentgenograms, the most effective treatment is evacuation of the focus.

Grossly, the calcified material which is found in early shoulder lesions feels oily and has been likened to sebaceous material. This material and also bits of tendon from nearby areas have been treated with fat

stains but neither free fat nor soaps could be demonstrated. When the material is analyzed it is found to contain calcium phosphate and carbonate in about the same proportion as is found in bone.

What is probably the most characteristic lesion is what may be termed "calcium granuloma." This is a focus of calcium containing necrotic tissue debris, usually large in size, which is surrounded by a wall of granulation tissue. The wall consists of fibroblasts, small round cells, macrophages, and small foreign body giant cells in varying proportions. Intense edema with fibrin and leucocytic infiltration in the tendon substance was not noted, but in a few instances in which the calcium deposit involved the musculotendinous junction evidences of acute inflammation were seen. The muscle showed evidence of degeneration, fragmentation, and infiltration with leucocytes and round cells. Apparently the presence of an adequate blood supply in the vicinity is necessary for the production of an acute inflammatory reaction. In some sections, in a single low power field, it was possible to see the progressive stages of degeneration from normal tendon through hyalinization, fibrillation, and the formation of rice bodies. In addition to the degeneration of collagenic fibers there was degeneration and fragmentation of cells in the area. The larger cystlike cavities in the tendon, which contained the white calcium-containing fluid, or paste or chalklike material, were believed to be the result of progressive degeneration of the tendon, either from a single focus or formed by the coalescence of two or more spreading foci.

C. FRED GOERINGER. M.D.

Osteochondritis Dissecans of the Head of the Ulna. JOHANNES THOMS. *Acta radiol.*, Stockh., 1950, 34: 161.

The various sites which may be involved by osteochondritis dissecans are enumerated. A report is made of a case affecting the head of the ulna, a localization which does not appear to have been reported earlier. The author claims that the lesion was caused by an injury sustained 3 years previously. The patient had had an injury so severe as to cause a greenstick fracture of the radius, but the ulna, and particularly the head of the ulna, failed to show any signs of fracture. Since this first injury, the patient had noticed symptoms from the wrist when it was strained. A new injury, 3 years later, gave rise to severe symptoms in the wrist in the form of swelling, tenderness, and pain on motion. On the subsequent day a fully developed osteochondritis dissecans with sequestration was diagnosed. The osseous development had been found to be normal at previous examinations, but osteochondritis dissecans was not demonstrable in joints other than the injured one. The roentgen film of the left wrist indicated a semicircular defect in the joint surface of the head of the ulna. The defect had smooth borders, and in its center there was a loose, slightly irregular sequestrum the size of a wheat grain. No bony changes were found in the radius.

Fig. 1 (Thoms). Roentgenograms showing the patient's wrist 3 years after fracture was incurred. Diagnosis: osteochondritis dissecans of the head of the left ulna. Loose body in the left wrist.

According to Brickley and Grow, more than 85 per cent of the reported cases have involved the knee joint. Next in order of frequency is involvement of the capitulum humeri or of the medial femoral condyle. The lesion rarely involves other sites. C. FRED GOERINGER, M.D.

Lesions of the Intervertebral Fibrocartilage from the Point of View of the Orthopedic Surgeon (Las lesiones del fibrocartílago intervertebral: punto de vista del cirujano ortopédico). A. INCLÁN, JR. *Cir. ortop. traumat.*, Habana, 1950, 16: 18.

During the past 4 years the author and his father, Professor A Inclán, have observed in their private practice 98 patients complaining of sacrolumbalgia, with or without sciatalgia. In 33 of these sufferers a diagnosis of probable discal hernia was made.

In 15 instances the spinal canal was explored through the interlamellar space without laminectomy. In 3 of these cases the preoperative diagnosis was not hernia of the disc. Of the remaining 12, the discal injury was confirmed by exploratory operation in 11. In 8 of these 11 cases other skeletal lesions, sufficient to produce a part of the symptoms, were observed. These associated lesions included spinal articular anomalies leading to vertebral insufficiency, hypermotility of the vertebrae, spina bifida, and degenerative arthritis.

As a rule a careful study of the patient will suffice to locate the injured disc; myelography was done in only one instance in this material. Pantopaque was the opaque substance used. The symptoms present in these cases were sacrolumbalgia (100 per cent), sciatalgia (100 per cent), increase of pain on coughing (90 per cent), a history of violence or trauma (75 per cent), zones of cutaneous hypesthesia (33 per

cent), muscular atrophy (41 per cent), positive Lasegue's sign (66 per cent), diminution of the reflexes of the knee or of the Achilles tendon, or both, (75 per cent), and narrowing of the intervertebral space on the roentgenogram (66 per cent).

Spinal fusion was done in 92 per cent of cases. The methods employed were those of Hibbs, or of iliac or tibial implants, fresh or preserved by congelation. In practically all of these cases the author employed internal fixation with vitallium screws through the spinal articulations, according to the method described by Ruiz in 1940. This last method is recommended as assuring an absolute immobilization of the vertebrae for a sufficient time to permit the development of bony consolidation.

These patients, reporting after periods of 2 to 24 months postoperatively, indicated disappearance of the symptoms with functional restitution in 87 per cent, and mild residual symptoms without functional incapacitation in 13 per cent; there were no instances in which the condition was not improved, and none in which it was aggravated.

Reoperation has in no case been necessary; in fact, the author believes that with proper fusion the discal hernia cannot recur.

JOHN W. BRENNAN, M.D.

Subcutaneous Rupture of the Tendo Achillis. THOMAS H. BATE. *Arch. Surg.*, 1951, 62: 14.

The author was able to collect 14 cases of subcutaneous rupture of the tendo achilles, from the foreign and English journals, to which were added 2 cases of his own, which made up the total number (102) of cases in the world's literature. The condition may be classified as follows:

1. Pathological subcutaneous rupture. This results from minimal trauma, at times so slight that it may pass without notice by the patient.

2. Traumatic subcutaneous rupture. Direct trauma as the cause of subcutaneous rupture is reported in the literature not nearly as frequently as sudden contracture of the triceps surae muscle.

In cases of pathologic rupture the patient usually complains of little pain at the time of the accident. Walking, if possible, is painless, as well as palpation and any sort of passive movement which may be made. Palpation usually shows a depression.

With the traumatic rupture, pain is an infallible symptom of capital importance.

The immediate functional disability is variable and is in direct relation to the pain. There are patients who cannot rise, and, after being helped to their feet, cannot walk. On the other hand, there are patients in whom the pain is not so sharp. These persons are usually able to get up under their own power, place their rigid foot at right angles and walk without difficulty, using small steps and dragging the foot. It has been said that the spontaneous pain diminishes in intensity as time passes.

Ecchymosis is almost never absent but it may be present in varying degrees. Usually the discoloration occupies the posterior part of the heel, reaching to both malleoli. A pathognomonic sign is the presence of a depression and in many cases coagula and edema fill it and mask the diagnosis, especially when a number of days have elapsed since the accident.

In view of the functional results of the operation, in particular the early results, the operators preferred operative intervention. Use was made of steel sutures which were removed at the completion of healing.

A molded boot is applied at the termination of the operation. The boot is removed at the end of 5 to 7 days, the skin sutures are removed, and a walking iron is applied. In 3 weeks the walking iron and steel sutures are removed. A brace is used for the next 2 months. C. FRED GOERINGER, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Shelf Operation for Congenital Subluxation and Dislocation of the Hip. MARTIN E. ANDERSON and WILLIAM H. BICKEL. *J. Bone Surg.*, 1951, 33-A: 87.

The term "congenital dysplasia of the hip" is used to describe a group of developmental malformations of this joint. The chief abnormalities consist of a shallow acetabulum whose outward prolongation is deficient and of associated hypoplasia of the head of the femur. Hypoplasia and anteversion of the femoral neck and torsion of the shaft of the femur also have been noted in this condition. When the acetabulum is not sufficiently deep to accommodate the head of the femur in the weight-bearing position, there may be incomplete displacement (subluxation) or complete displacement (dislocation) of the head of the femur from the malformed acetabulum.

The cases reported in the complete paper represent the results of only one form of treatment of a late phase of congenital malformation of the hips. The purpose of the shelf operation is to afford a stable weight-bearing ledge to support the pelvis on the head of the femur.

Ghormley's procedure was described in detail by the authors because it was used, with minor exceptions, in all the shelf operations reported in their study. Ghormley stressed the importance of (1) heavy traction for several days before operation, or at the time of operation, to reduce the dislocation or to bring the head of the femur as far down as possible, and (2) building a shelf which is large enough to cover the head of the femur without interfering with abduction by abutting against the trochanter. The anterior portion of the iliac crest and margin of the acetabulum are exposed through a lateral incision which is curved posteriorly.

The cases selected for study included all patients (76) on whom shelf operations had been performed because of congenital dislocation or subluxation of the hip during a 10 year period (January, 1936 through December, 1945) at the Mayo Clinic.

Roentgenograms taken before operation were studied to classify abnormalities of the acetabulum and

of the head and neck of the femur. Measurement of the C-E angle was found to be useful in classifying various degrees of dysplasia and subluxation of the hips. The roentgenologic features of both hips of each of the 70 patients were studied. In the 60 cases in which a unilateral shelf operation was performed, abnormalities of the opposite (unoperated) hip were noted in 23 cases, or 38 per cent. Only 37, or 26 per cent, of the entire group of 140 hips studied (70 cases) could be classified as completely normal.

The functional status of each hip was estimated from records of the examination made before and after the shelf operation had been performed. No attempt was made to evaluate the result of the operation in a case in which the follow-up period was less than 1 year. The follow-up period varied from 13 months to 13 years and 2 months. The average duration of the follow-up period for the group of 70 patients was 4 years and 8 months. It was possible to re-examine 43 of these patients within the follow-up period. Information for the follow-up study was obtained by letter from the other 27 patients.

A completely satisfactory method of classifying the results of the shelf operation is difficult to devise. The authors estimated the patient's degree of functional impairment as regards limp, fatigue, pain, and stiffness before and after operation. In determining the functional status of the individual, each symptom was graded on the basis of 1 to 4, in which 1 represents a slight, and 4 a very severe degree of impairment. Absence of the symptom was shown by the figure "0." In a series of 80 operations for congenital subluxation or dislocation of one or both hips, 58 operations (72.5 per cent) were successful in that the patients were partially or entirely relieved of limp, pain, and hip fatigue while retaining a good range of motion in the operated hip. Twenty-two of the operations (27.5 per cent) were unsuccessful in that the patients' symptoms were unimproved. Poor results were attributed to construction of shelves which were inaccurately placed, were too small or were absorbed. Arthritic symptoms persisted or developed after operation in a few instances.

Arthroplasty of the Hip Joint (Zur Arthroplastik des Hueftgelenkes). M. MUELLER and T. SIBAY. *Zschr. Urol.*, 1950, 80: 8.

Comparison is made between the use of the vitallium capsule according to Smith-Petersen and the ossacryl prosthesis according to Judet. On the basis of more than 300 arthroplastic operations on the hip joint during the past 3 years at the Anna Clinic in Leiden, Holland, the authors have come to prefer the plastic prosthesis of Judet to the vitallium capsule.

When the ossacryl plastic prosthesis is used the joint is amply exposed through a Smith-Petersen-Mathieu incision, the head of the femur is dislodged by the usual technique and ground down to fit the prosthesis (this involves removal of about half the head of the femoral bone), and the neck is perforated by a Steinman nail at an angle of at least 140 degrees as a mild degree of coxa valga is desired. An electric drill may assist in preparing the canal to receive the prosthesis, that is, to produce a diameter of 13.5 cm. The acetabulum is hollowed out and smoothed. The shaft of the prosthesis should extend beyond the hole in the subtrochanteric opening of the canal. The prosthesis is driven down into the canal with a hammer, the plastic head being protected by gauze. The transparency of the plastic permits a visual control in the procurement of complete contact between the bone and the prosthesis. Special mobilizing apparatus is employed in the after-treatment.

In the Anna Clinic of Van Nes the indications for arthroplasty of the hip joint have been so increased that arthrodesis, except in cases of coxitis tuberculosa, is scarcely ever considered. Even in this condition the old well-healed tuberculous hips may be treated by this method of arthroplasty.

JOHN W. BRENNAN, M.D.

The Nailing of Intertrochanteric Fractures (Nagelung pertrochanterer Oberschenkelbrueche). WALTER EHALT. *Zschr. Urol.*, 1950, 80: 3.

This report, of a more or less preliminary nature, is from the industrial City of Graz, Austria, and pertains to the use of a new type of fixation for the intertrochanteric fracture. The general appearance of the internal splintlike brace is shown in the original article.

The author uses a Neufield type of nail with a directing wire and three braces with angles of 125, 130 and 135 degrees, respectively. With the aid of the wire lead the nail is driven part way into the outer surface of the trochanter and then the brace is attached by means of its two screws which embrace each side of the head of the nail. The nail is then driven into place, the screws holding the brace to the femoral shaft are introduced and tightened, and then the screws about the neck of the nail head are tightened.

So far this method has been used 14 times on this type of fracture. The patients included 1 individual under 30 years of age, 1 in the fourth decade, 2 persons in the fifth decade, 2 in the sixth, 4 in the seventh, and 4 who were over 80 years of age. One woman of 82 died on the day following the operation from a cardiac attack, and in 1 case a mild superficial wound infection developed; all the other wounds healed per primam. The patients were allowed to be up and about after 3 or 4 weeks and from then on dispensed with crutches or other means of supplemental support. In every instance the result has been osseous union with practically free hip joint movement. Since the knee joint has been fixed by an extension apparatus, it has also remained freely mobile.

There were 2 old intertrochanteric hip fractures belonging to Boehler's group 4. One of the patients was 64 years old with refracture 3 months after the accident; the other was 71 years old with refracture 6 weeks after the accident. The treatment of these 2 patients differed from that of the others in that the

nailing and bracing were preceded by open reposition of the fracture (a difficult job). Even in these cases the postoperative course was smooth and the union osseous, and the movements of the hip joint were practically unhindered.

The nailing is technically simpler than that in cases of fracture of the femoral neck, since the nail need not be directed so exactly in the long axis of the neck. It must, however, grasp a sufficient amount of the massive portion of the head and neck. Here again it is not so important to fit the end of the nail with relation to its distance from the joint surface. The author thinks it is better to place the nail in the lower region of the neck, as in this manner a thicker part of the outer massive portion of the trochanter is grasped. JOHN W. BRENNAN, M.D.

Bone-Shortening for Inequality of Leg Lengths. A. L. EYRE-BROOK. *Brit. M. J.*, 1951, 2: 222.

The author attempted to demonstrate that leg shortening has more to recommend it than other forms of leg length equalization.

Bone-shortening is the preferable approach to all cases with exception of the few in which patients are unwilling, or who can ill afford, to sacrifice any height.

Some surgeons seem far more willing to practice leg shortening by epiphysiodesis than to attack an older patient by surgical bone-shortening, logically the equivalent operation for an older age group.

A very thorough technique is required in epiphysiodesis to avoid deformities, and epiphysiodesis is often performed at too late an age for the desired results to be obtained.

Surgical bone-shortening is a safe procedure, and is certain and quick in its results.

It is preferable in the femur, and two methods are advocated: (a) straightforward lateral overlay with transfixing screws; (b) excision of a segment below the lesser trochanter and fixation with a Blount plate.

Two examples of a 4 inch femoral shortening with full return of knee movement and control within 3 to 5 months are reported. C. FRED GOERINGER, M.D.

FRACTURES AND DISLOCATIONS

Tetraethylammonium Chloride in the Process of Fracture Healing. (Il tetraetilammonio nel processo di guarigione delle fratture). ANTONIO PAPA and BRUNO BUONOMO LA ROSSA. *Gior. ital. chir.*, 1950, 6: 611.

With the knowledge that tetraethylammonium chloride, administered parenterally, blocks the transmission of nervous impulses across autonomic ganglia with a resultant increase in peripheral circulation, the authors studied the effect of this drug on the process of the healing of fractures in a series of experiments on rabbits.

The rabbits, 16 in number, were approximately of the same age and were kept on a regulated diet during the entire experiment.

The animals were divided into two series of 8 each. In both series, a fracture between the medial and upper thirds of the radius was produced through a surgical incision under ether anesthesia. The operative wound was sutured and protected by a sterile dressing. No immobilization was done. Five of the animals were treated with intramuscular injections of 25 mgm. of tetraethylammonium chloride per kilo of body weight; the remaining 3 were used as controls.

In the first series the injection was given every 24 hours, and in the second series it was given every 12 hours.

On the fifteenth day after the fracture had been produced, 2 of the treated animals and 2 of the controls were sacrificed. The fracture site was removed en bloc, prepared, and studied histologically. On the thirtieth day after the fracture had been produced, 2 of the treated animals and 2 of the controls were sacrificed, and similar histologic studies were made. Thirty days later all the remaining animals were sacrificed and studied. On the tenth, twentieth, and thirtieth days, respectively, after the fracture had been produced, roentgenograms of all the animals were taken.

In the first series of rabbits, x-ray films taken on the tenth day after fracture of the treated animals showed an indistinct fracture line with moderate ossification of the interfragmentary callus and a thin covering of ossification of the periosteal callus. X-ray films of the controls showed an indistinct fracture line with no ossification of the interfragmentary callus.

Twenty days after the fracture, x-ray films showed definite ossification of the interfragmentary and periosteal callus. In the controls, there was incipient ossification of the interfragmentary callus.

In the second series, x-ray films taken 10 days after fracture in the treated animals showed loss of bone substance with the outline of the fragments, especially that of the superior fragment, slightly disappearing. First, signs of ossification of the interfragmentary callus appeared. X-ray films of the controls showed no evidence of ossification of the interfragmentary callus.

Twenty days after the production of fracture, x-ray films of the treated animals showed intense ossification of the interfragmentary callus and also of the periosteal callus.

Thirty days after the fracture, x-ray films of all the treated animals showed a very advanced ossification of the interfragmentary and periosteal callus. Signs of the break had practically disappeared. In the controls, calcification of the interfragmentary and periosteal callus was seen, and the whole fracture line could be definitely seen.

The following histologic findings were observed from prepared slides:

Slides made from tissue removed from treated animals 15 days after fracture showed that the callus had proceeded to the cartilaginous stage, although not all of the connective tissue had disappeared from

the callus. Just under the periosteum there were some bundles of fibrous tissue, while in the medullary canal there were numerous areas of cartilage. No signs of necrosis were seen at the site of the fracture.

The callus of the fractures of the control animals differed from that of the treated animals in that there were few signs of cartilage cells and there was a preponderance of connective tissue cells in the region of the periosteum. In addition, there was an abundance of small-cell infiltration. Some areas of focal necrosis were observed.

Thirty days after fracture, the treated animals showed an advanced stage of ossification of the fracture. The newly formed bone was of normal constituency. There were few areas of cartilage. In the area of the medullary canal, bony trabeculae presented a normal appearance. No permanent areas of cartilage were seen. At the line of fracture, newly formed bone could not be distinguished from pre-existing bone.

The tissue from control animals, 30 days after fracture, showed numerous cartilaginous areas with sparse areas of bony tissue. In the area of the medullary canal, no trabeculae of bone were seen.

In the second series of animals treated with 25 mgm. of tetraethylammonium chloride per kilo of body weight every 12 hours, the following results were shown, by study of histologic slides:

Fifteen days after fracture, the treated animals showed an advanced stage of ossification, from connective tissue to cartilaginous phase. There were more numerous areas of cartilage in these animals than in similar animals of the first series. There were numerous areas of osteogenic tissue present, but there were no areas of necrosis at the fracture line.

In the control animals of the second series, 15 days after fracture, slides showed that the callus was made up of connective tissue for the most part, with sparse areas of cartilaginous tissue.

Thirty days after fracture, sections of the treated animals of the second series showed complete bony repair with uniform regularity of the newly formed bony tissue. At the fracture line, the newly formed bone could not be distinguished from the pre-existing bone.

The controls of this series showed a definite retardation of progress from the cartilaginous to the bony stage. There were few areas of osteoid tissue among the cartilage.

Both the x-ray and histologic findings indicate that greater rapidity in healing took place in the second series than in the first. The rapidity of elimination of the tetraethylammonium chloride shows that a better clinical result was obtained in the animals receiving injections at 12-hour intervals.

From their studies, the authors draw the conclusion that injections of tetraethylammonium chloride (preferably every 12 hours) favorably influence the healing of fractures, as evidenced by a rapid ossification of the fracture, and that the administration of this drug is indicated in cases of delayed repair.

BLACKWELL MARKHAM, M.D.

Conservative Treatment in Fractures of the Neck of the Radius (Die konservative Behandlung von Bruechen des Radiushalses). JOERG BOEHLER. *Chirurg*, 1950, 21: 687.

Fractures of the proximal end of the neck of the radius may cause permanent functional damage, especially inhibition of pronation and supination. Most authors recommend surgery if considerable displacement of the proximal end is present. Either extirpation of the head of the radius or open reposition, with or without osteosynthesis, is the treatment suggested.

The author describes a method of conservative reposition of these fractures. A Steinmann nail is introduced percutaneously, inserted between the fragments, and under fluoroscopic control the capitulum of the radius is lifted and brought in place. In this way the displacement is easily corrected.

The arm is put in a cast for 3 weeks with the elbow flexed at a right angle and the forearm in a position between pronation and supination. The nail remains in place only until the cast has hardened and is then removed.

WERNER M. SOLMITZ, M.D.

The Treatment of Pathologic Luxations of the Hip Joint. Indications, Technique, and Late Results (Trattamento della lussazione patologica dell'anca. Indicazioni, tecnica e risultati lontani). GIORGIO GHERLINZONI and CARLO PAIS. *Chir. org. movim.*, 1950, 34: 335.

The material reported consists of 353 patients with luxation of the hip joint observed at the Rizzoli Institute of Bologna, Italy, during the past 40 years, of which 181 were subjected to operation. In 164 the condition resulted from acute septic arthritis; 113 of these were treated surgically. In 4, it resulted from rheumatic polyarthritis and 3 of these were treated surgically. In 77 patients the condition resulted from tuberculous coxitis; 27 of these were treated surgically. In 1 case resulting from echinococcus infection, operation was unsuccessful. Of 4 patients with neoplasms, 1 with a destructive lymphangioma was operated upon with fair results. There were 5 patients with tabes dorsalis, of which 2 were operated upon. In 61 patients the dislocation resulted from poliomyelitis and, of these, 33 were subjected to operation. There was 1 patient with dislocation, among 190 patients with myopathy, who was not operated upon, and there was 1 patient with dislocation from cicatricial pull (due to a burn) who was subjected to operation. One patient among 23 with dislocation accompanying spastic paralysis was also operated upon, but of 12 with dislocation due to spina bifida none was operated upon.

In general, pathologic dislocations have become less extensive and less frequent with the advance of antibiotics and other forms of prophylactic therapy; there have been fewer contraindications to surgical therapy, and the late results of surgery have improved with better understanding of the capabilities of each type of surgical procedure.

The mobility of the joint which has been operated upon is most important, of course, in the instances of bilateral involvement. In addition to the unilaterality or bilaterality of the dislocation, the condition of the acetabulum and the extent of destruction of the upper end of the femur, the type and extent of involvement of the other joints, and the condition of the muscles and fascial structures of the hip itself and of the other portions of the body, will influence the indications for operation.

The cases of traumatic and congenital dislocation are excluded from the material. However, such material as has been reported in the medical literature, and pathogenetic, anatomic, and clinical factors, as well as such aspects of nonoperative therapy as would seem pertinent to the surgical aspects of treatment, are included.

Dislocation of the hip joint resulting from septic arthritis has been the most frequent type. The tendency of treatment has been toward simple reduction in the young child. This includes, of course, reconstruction of the joint combined with reduction. In the more inveterate and extensive processes there has been a preference, in the unilateral forms, for fusion operations. In the bilateral forms the preference is for the preservation of the mobility incident to the osteotomy of supportive type. In this last material ankylosis was already established in 4 instances and nothing was done except correction of the faulty direction of the ankylosed femur by directional osteotomy. In all of these patients the object of the operative procedure was successfully attained.

In those cases of tuberculous coxitis which were not reducible, or indeed curable, by continuous traction methods, the previous inclination to treat the lesion by exclusively extra-articular methods (iliofemoral or ilioischial fusion with transplant) has become less imperative with the advent of the antibiotics and methods of treating surgical shock. Resection may be considered together with reduction arthrodesis, even in the presence of intra-articular encysted abscess. Ankylosis is quite generally the aim, since this form of luxation of the hip joint is hardly ever bilateral. The authors had only 1 instance of bilateral luxation in a patient with coxitis and even in this case a cure was procured exclusively with orthopedic methods. The arthrodesic procedures should, as a rule, be preceded by articular resection to get rid of the exuberant granulations and the bone surfaces of low vitality.

The dislocations resulting from poliomyelitis are characterized by their rarity, by their almost exclusive unilaterality, and by their peculiar tendency toward recurrence of the luxation. This inconstancy of behavior demands a variety of therapeutic measures. Operative therapy is, of course, useless in those patients who will not be able to walk anyhow; simple reduction is practically useless and simple reduction with plastic capsular repair is in most cases inadequate. Work has been going on at the Institute with reference to the best method of combating the tendency toward recurrence of the luxation, especially that tendency resulting from outward rotation of the femur. It has been suggested from studies carried out on cadavers that the best method of combating the lateral rotation of the leg is to detach the lesser trochanter (the iliopsoas muscle is hardly ever paralyzed in poliomyelitis), pass it around in front of the femur, and re-attach it to that bone just beneath the greater trochanter. This procedure has not as yet been tested practically.

Arthrodesis will, of course, be indicated in the reduction of postpoliomyelitic dislocation of the hip joint, in which the extent of the paralysis would render reduction unstable on any account, and in which, even if the reduction should persist, the muscles would not be strong enough to take advantage of the residual mobility of the joint properly. The object of the operation was successfully obtained in 5 cases of this nature.

In inveterate cases which would no longer justify reduction attempts, some movement in the joint of the postpoliomyelitic hip may be retained by the supportive type of osteotomy. The resulting shortening of the limb may eventually be compensated by surgical measures. JOHN W. BRENNAN, M.D.

Primary Osteosynthesis in Compounded Fractures of the Bones of the Leg as a Surgical Problem (A propósito da osteosíntese primitiva nas fracturas expostas da perna). FORTUNATO LEVY and VICTOR REGALA. *Bol. clín. hosp. civ. Lisboa*, 1950, 14: 209.

Stimulated by the article by Stimson in the *American Journal of Surgery* for December, 1947, the authors have been treating fractures of the leg bones by immediate plating. During the past year and a half 6 of these fractures have been so treated.

In all these cases the plate used was ample, with large tightly fitting screws, sufficiently long to prevent torsion movements of the fracture ends. A cast was added for further assurance. Surgical toilet of the wound always preceded the operation and any evidence of contamination or of necrosis was removed, if necessary, by sharp dissection. The protruding bone was clipped when necessary to secure approximation of the fracture ends. The tissues were sutured shut over the plate in every instance; when necessary, collateral incisions were carried out. Antibiotics were, of course, used in the local treatment of the wound during operation and generally following this procedure.

Four of these injuries consisted of transverse fractures of the lower or middle thirds of the tibia and all these were plated, as was also a transverse break of the base of the right peroneal malleolus. The remaining patient had an oblique fracture of the lower third of the tibia with a wedge-shaped loose fragment. This injury was wired.

In all these cases the time which had elapsed between the accident and the operation ranged from 6 to 30 hours, that is, in excess of the time limit of 6 hours set by Friedreich for the application of a

method of treatment requiring absence of infection; yet all these breaks healed without complications of serious nature and within the usual time required for closed fractures. The skin wound always healed within 12 to 20 days. In 1 patient an extensive necrosis of the skin required skin grafting. The metallic fixation was always removed after healing of the bone break.

In 1 instance both tibias were broken; the one was subjected to plate fixation in the manner described, and the other was treated by Kirschner wire suspension. The plated tibia healed sooner than the tibia on the opposite side; in other words, the firmness of the immobilization of the method did not seem to produce any tendency toward the development of pseudarthrosis.

Of course, not all cases are proper for the procedure; breaks with extensive comminution or contamination would hardly be regarded as suitable. However, when used, the method of immediate plating has the advantages of preventing secondary infection and of osteomyelitis which is believed to be the result of improper fixation, and of markedly shortening the period of disability. JOHN W. BRENNAN, M.D.

ORTHOPEDICS IN GENERAL

The Cure of Experimental Scoliosis by Directed Growth Control. I. WILLIAM NACHLAS and JESSE N. BORDEN. *J. Bone Surg.*, 1951, 33-A: 24.

The experimental production of spinal curvature in animals is based on four facts: (1) that vertebral bodies grow in height by the activity of their epiphyseal cartilages, (2) that epiphyseal growth can be retarded by compression, (3) that the power of growth persists after the compression is removed, and (4) that unequal elongation of the two sides of the spine will result in spinal curvature. These principles have been applied by the unilateral clamping of several lumbar vertebrae in growing dogs. The clamp is so inserted that the epiphyses are not injured. The compression force is developed by the normal growth of the spine against the restraint of the clamp. In puppies so prepared, lateral curvature develops after 6 to 8 weeks and the deformities are remarkably like those seen in children.

Roentgenographically, they present wedging of the vertebrae and unilateral narrowing of the intervertebral spaces. If the clamp is removed after the curve has been established, the deformity persists or even increases.

Six dogs with fixed rotatory lateral curvature of the spine were subjected to selective growth control. The animals were still in the growing age. Their deformities had been produced by the stapling technique here described. The stability of these deformities were tested as follows: varying periods of time were allowed to elapse between the curve-producing and the curve-correcting phases of the experiment.

The treatment used consisted in clamping together the vertebrae in the primary curve on the convex side. With the animal in the prone position, a paraspinal incision was made in the lumbar area on the convex side of the spinal curve and was deepened to expose the sacrospinalis muscle. This was split bluntly over a line connecting the tips of the desired transverse processes. Periosteal elevation medially brought to view the junctions of these processes with the neural arches. Here a perforator was driven anteriorly and medially in the predetermined vertebrae, and the prongs of a staple were introduced into the prepared holes, so that the bodies of the vertebrae were entered without damage to the epiphyses. Closure of the soft tissues was then made in layers, and after a short postoperative recovery period, the animals showed no ill effects or disabilities attributable to the operation.

On the basis of the rotatory lateral curvatures in 23 normal growing dogs produced by unilateral lumbar growth restraint, the development of a similar deformity in 1 animal with thoracic stapling, and the correction of deformed spines under selective growth control in 6 dogs, it is obvious that a tool is available for the making and straightening of spine deformities. The author concluded that the human being should react to directed growth control since his vertebral bodies gain height by epiphyseal structures. C. FRED GOERINGER, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Some Phases of Diagnosis in Peripheral Vascular Disease. C. ALEXANDER HATFIELD and MARIO V. TRONCELLITI. *Surg. Clin. N. America*, 1950, 30: 1585.

The causes of peripheral vascular diseases may be classified as venous, arterial, and neurogenic. This article is concerned with various temporary means of relieving vascular spasm caused by sympathetic overactivity in these conditions. This may be accomplished by mechanical, systemic, or nerve block methods. The mechanical means include an intermittent pressure boot, or venous occlusion, and the oscillating bed. The systemic means include increasing the body temperature, general anesthesia, the intravenous administration of procaine, alcohol, or ether, priscoline hydrochloride, and tetraethylammonium chloride. The disadvantage of this method is that all the sympathetic nerves are affected rather than the parts involved. Nerve blocks accomplish optimal vascular dilatation of the involved vessels, and very little, if any, systemic reaction. The blocks most commonly used are lumbar, upper thoracic, peridural, and of the stellate ganglion. Accidental sensory anesthesia may be misleading and should, therefore, be avoided. Subjective relief following block furnishes good evidence of sympathetic paralysis.

The authors prefer 1 per cent procaine and, when possible, use an operating or anesthesia room; they give a barbiturate as premedication, and tell the patients about the procedure. Indications for block of the upper extremity include Raynaud's disease and Raynaud type phenomena as in thromboangiitis obliterans, and pneumatic tool or vibratory tool disease, as well as mechanical derangements in the root of the neck, as the scalenus anticus syndrome, cervical rib, causalgia, vasospasm with thrombosis of the brachial artery, and spontaneous thrombosis of the axillary vein. In the lower extremities, lumbar or peridural blocks may be used for embolus of a major artery, after embolectomy, and in cases of impaired circulation due to arteriosclerosis, diabetes mellitus, thromboangiitis obliterans and deep venous thrombosis, and thrombophlebitis.

The authors conclude that sympathetic anesthesia gives information for the diagnosis of the disease, affords symptomatic relief, and may be curative itself; a satisfactory temporary response is a valuable indication for permanent sympathetic denervation.

ALBERT M. SCHWARTZ, M.D.

Superficial Varices of the Leg (A propos des varices superficielles du membre inférieur). RENÉ VAN HOVE. *Acta chir. belg.*, 1950, 1059: 729.

The author reviews the clinical signs and tests utilized in examining varicose veins:

1. A positive Schwartz sign or test by percussion. In the presence of nonfunctioning valves, percussion of the distended vein with the patient standing upright gives a transmission impulse upward to the femoral region. Normally a vein does not transmit this impulse.

2. The Trendelenburg test consists of elevating the leg and compressing the saphenous trunk in the femoral region, which should, in the absence of perforation, maintain a collapsed distal saphenous segment if the test is negative. Should the test be positive (i.e., the distal segment of the saphenous veins fill), there is then evidence of communicators or perforating veins, and regurgitation backward into the saphenous vein. An elaboration of this test by the placement of several tourniquets at various levels to ascertain the approximate site of deep communication is called the MacLean and Slevin Test.

3. The Perthes test consists of vigorous muscular exercise with the tourniquet applied, resulting, if negative, in a milking effect with collapse of the varicose veins if the deep circulation is patent. This test is positive if a collapse of the peripheral varicose veins does not occur.

4. Manometric studies. With a needle placed in an important varix, it is possible to make and record a qualitative estimate of the backflow from the saphenous column—or by the use of tourniquets, from the communicating deep veins, when estimations are made at various levels in the leg.

5. Phlebographies. With the use of 40 c.c. of umbradil injected into the dorsal vein of the foot, it is possible to ascertain definitely the permeability of the deep venous circulation.

The author attempts to evaluate the effect of prolonged standing on the development of varicose veins. Citing, for example, bicyclists, the author believes that prolonged intra-abdominal pressure is largely responsible for varicosities, and (with a manometer) in distended veins they were able to demonstrate 100 per cent increase in pressure within the leg veins by voluntary abdominal pressure.

A prolonged dissertation on hydrodynamics is presented, and finally the authors elaborate on the varicose diathesis to account for the prevalency of varicose veins.

JANE C. MACMILLAN, M.D.

Sequelae of Phlebitis of the Lower Extremities (Les séquelles des phlébites des membres inférieurs). R. TINGAUD. *Sem. hôp. Paris*, 1950, 26: 4500.

In addition to changes in the skin and the soft tissues (such as muscles, ligaments, and aponeuroses) osseous, nervous, and vascular lesions also play an important role in the postphlebitic syndrome.

Diffuse osteoporosis is not infrequently found in roentgenograms of the involved extremity.

Nerve fibers may participate in inflammatory processes, or their compression by edema may be

responsible for painful manifestations. Sclerotic lesions are always found in the regional sympathetic glands.

Arterial lesions seldom lead to thrombosis but arterial spasm is undeniable and may produce so-called blue phlebitis. There is no doubt that capillaries are always involved. In the early stages their functional lesions are reversible. Edema of the affected extremity interferes with the lymphatic circulation, thus creating a vicious circle. The familiar changes in the venous trunks represent the most important lesion. Phlebography has established the fact that thrombus formation is a reversible process and that an occluded vein may become permeable. However, such a vein has rigid walls and its valves are permanently destroyed.

French authors are of the opinion that 60 per cent of thrombi occur in the femoral region, followed in the descending order of frequency by the popliteal, iliac, and calf regions.

After acute phlebitis the plasma volume is diminished and the density of the plasma is increased for a long time. These changes may or may not be accompanied by an increased prothrombin content of the blood.

As to the interpretation of the findings in chronic phlebitis, the mechanical and the nervous theory supplement each other.

If the thrombus is extensive and is not located in one of the two critical zones, namely, the popliteal vein or the common femoral vein above its junction with the saphenous vein, edema is chiefly of vasomotor character; amelioration may be expected from conservative treatment. If the thrombosis is extensive and occupies one of the two critical zones, the collateral circulation is insufficient, the edema is mainly of mechanical character, and vasomotor therapy will fail. If the thrombosed segment of the vein becomes permeable, high venous pressure will lead to engorgement of the capillaries, edema, local anoxemia, and ulcerations.

Results of ascending and descending phlebography and determination of the venous pressure suggest proper treatment. The last-mentioned method is applicable only if the vein is patent and its valves are insufficient. If the oscillometric index is abnormally low or if there are signs of blue phlebitis or intermittent claudication, arteriography is indicated.

The prophylactic treatment consists of the administration of anticoagulant drugs, early mobilization, the application of elastic bandages, and intra-arterial injections of drugs affecting the sympathetic system. The author is skeptical in regard to the value of venous ligations.

Conservative curative treatment consists of intra-arterial injections of novocain which may alleviate pain and edema in mild cases. This method may be supported by the application of elastic bandages and physiotherapy. Injections of sclerosing solutions may be considered only after phlebographic studies. Great caution should be exercised in their employment. Thermal baths exert a beneficial effect on edema and cellulitis, and in a lesser degree on trophic changes and ulcerations.

Resection of the thrombosed segment furnishes good results if it is done at an early stage and if the lesion is well circumscribed. Sufficient time has not elapsed to evaluate resection of the entire saphenous vein. Pain may be relieved by lumbar sympathectomy which, however, should be supplemented by phlebectomy if an effect on edema is expected. The anastomotic system between the popliteal vein, on one hand, and the veins of the thigh and the lower leg, on the other hand, is very poor. Inasmuch as the weight of the blood column in an incompetent vein aggravates the condition of the involved leg, a thrombosed popliteal vein which subsequently became patent should be resected.

JOSEPH K. NARAT, M.D.

The Syndrome of Isolated Thrombus of the Anterior Tibial Artery, and Its Treatment (Le syndrome de la thrombose isolée de l'artère tibiale antérieure, et son traitement). RENÉ LERICHE. *Presse méd.*, 1950, 58: 1285.

Thromboses appear to have a predilection for certain sites, among which are the deep femoral artery and, more rarely, the superficial femoral artery, especially the segment within the adductor canal, the posterior tibial artery frequently, and the anterior tibial artery rarely. In a total of 2,000 arterial operations, the author has encountered occlusion of the anterior tibial artery but twice. The clinical pictures were so characteristic that they were considered worthy of description.

Both patients were elderly males suffering from sudden pain in the anterolateral portion of the leg, inability to walk, and no association of intermittent claudication, but with pain on movement, and inability to stand upright. At the end of several days the appearance of the leg was striking. The leg was held in varus position and movement of the foot and toes was impossible. The anterolateral surface was painful and tender; the color was normal except for several erythematous skin areas that blanched with pressure. The posterior tibial pulse was barely susceptible in one case, but both pulses were normal in the second case.

In both cases Leriche attempted to aspirate the vessel before exploration, and with the discovery and removal of massive clots in the anterior tibial artery amputation was avoided.

JANE C. MACMILLAN, M.D.

Thrombosis Obliterans of the Abdominal Aorta and the Syndrome of Leriche (Trombosi obliterante dell'aorta addominale e sindrome di Leriche). E. BENEDINI. *Ann. ital. chir.*, 1950, 27: 713.

Four cases of the so-called syndrome of Leriche are reported. In 3 of these patients, the findings at autopsy or at operation provided evidence of the actual conditions present in the terminal aorta and its bifurcation, and in the more distal branches. In the fourth patient, amputation at the thigh for gan-

grene of the foot has been the only surgery performed. This patient is the only patient who has survived and is still in the hospital under observation. In this patient, however, the symptoms (claudication, pallor, myatrophy of the extremities, sexual impotence) and the clinical course indicated the presence of obliterative aortitis.

Great emphasis is placed on the presence of *impotentia erigendi* without loss of libido. In 3 of these patients such impotence had been present for periods of 6, 7, and 5 years respectively. In the remaining patient such impotence is not mentioned; however, we know from the literature that not all patients with the syndrome of Leriche are impotent and that such impotence has been cured by resection of the iliacs and bilateral lumbar sympathectomy (Morel: *Presse méd.*, 1949, 157: 12). Finally, the author recalls a patient—not here reported—who was typically impotent in the sense of the syndrome of Leriche, and yet at autopsy the thrombotic process was limited to the vessels peripheral to the aorta, iliacs, and spermatics. All this rather disposes of the original idea of Leriche that the impotence in these cases is due to thrombotic co-involvement of the spermatic arteries.

Another sign of differential diagnostic significance is the presence of palpable pulsations in the aorta above the umbilicus, and their absence beneath the navel; here, however, the author does not subscribe to the belief that the presence of pulsation below the umbilicus necessarily excludes the presence of the aortoiliac thrombotic process.

The character of the histologic and gross anatomic findings on the arteries in this series of cases points to a long-standing thrombotic involvement distally, and a tendency for the thrombosis to grow centrally until eventually the renal arteries (or even the celiac arterial plexus) are reached, resulting in death of the patient. In all these cases the processes of long standing were low down near the aortic bifurcation, or even in the iliac arteries, and the more recent appearing processes were more proximally located. In the 3 arterial trees here examined, there were always present at some point in their course advanced arteriosclerotic or atheromatous changes, and in 2 there were also present evident nonspecific inflammatory findings (small cell infiltrations) in all the vascular layers, but particularly marked in the media and adventitia. In one of these patients, despite a full-blown Leriche syndrome and an advanced degree of arteriosclerosis, there was no evidence of inflammatory reaction in the vascular walls. This finding, of course, indicates that some doubt is justifiable with reference to the theory of the Leriche school that the initial lesion is an inflammation of the adventitia and media with secondary spasms, intimal hyperplasias, and thromboses.

Although the author seems to negate the theories as to the etiologic significance of inflammation, and favors the factor of arteriosclerosis, he does not seem to doubt its pathogenic importance, including the effects of arterial spasms on the efficacy of development of the collateral circulation in these patients. He believes that his experience justifies the performance of excision of the thrombosed vessels, which operation was recommended by Leriche for the purpose of eradicating these very spasmotic impulses. The author also recommends the excision of the first, second, and third lumbar sympathetic ganglia bilaterally.

The greatest improvement, however, is to be expected in procuring the patients in a less advanced condition of their arterial lesions. Here the frequency of insidious development of the lesion is to be deprecated, and may be so pronounced as to leave the detection of the early process the sole responsibility of arteriography of the aorta.

Although professing no experience in the matter, nevertheless the author is enthusiastic about the possibilities of the disobliteration method introduced by Dos Santos. JOHN W. BRENNAN, M.D.

A Graft of the Preserved Human Aorta (Greffe d'aorte humaine conservée). CH. DUBOST, N. O. ECONOMOS, M. DURAND, and C. METIANU. *Sem. hôp. Paris*, 1950, 26: 4497.

Gross of Boston was the first to employ an arterial graft in the treatment of the tetralogy of Fallot and of coarctation of the aorta. The authors operated on a woman aged 26½ years, in whom a diagnosis of hypertension and stenosis of the aortic isthmus had been made. The operation showed that the subclavian artery was also involved in the stenosis. After resection of the stricture it was impossible to approximate both ends of the severed blood vessel and therefore a segment of aorta, 5 cm. long and which had been preserved for 3 days, was grafted, with Deknatel silk No. 000. Angiocardiography performed 50 days after the intervention failed to reveal any signs of stenosis. The authors conclude that blood vessel grafts should always be on hand because preoperative angiocardiography may fail to reveal the extent of the stricture. In view of the fact that the diameter of the subclavian artery in the authors' case was considerably reduced, Blalock's or Clagett's procedure did not come into consideration.

In another patient with the tetralogy of Fallot, a graft, 6 cm. long and preserved for 10 days, was placed between the subclavian and the pulmonary artery. In the third patient with the same condition, a graft preserved for 24 hours was used for a terminolateral anastomosis. Both patients recovered. Preserved artery appears to be superior to an autoplastic or a heteroplastic venous graft.

An arterial graft was also successfully employed for the repair of a defect created by resection of a 15 cm. long segment of the external iliac artery. The resection was performed because of thrombosis and segmental arteritis.

The authors conclude from their observations that arterial banks should be created wherever cardiovascular surgery is performed.

JOSEPH K. NARAT, M.D.

Graft of the Aortic Bifurcation in Dogs (La greffe du carrefour aortique chez le chien). JACQUES DALEM. *Acta chir. belg.*, 1950, 49: 759.

Since aortography was introduced in our diagnostic armamentarium the syndrome of thrombosis of the terminal aorta and its branches has been studied more closely. In view of the serious sequelae of this condition and especially the danger it entails for the renal arteries, surgery is the treatment of choice in many cases. At the present time, resection of the occluded portion and sympathectomy is the usual procedure. Grafting of the aorta and the bifurcation has not been attempted yet in man.

In numerous experiments on dogs the author studied whether it is possible to replace the entire terminal aorta with its branches by grafting.

In the first group of experiments the author studied the effects of temporary obliteration of the abdominal aorta. In a series of 10 dogs the aorta was clamped with a Blalock clamp distally to the renal arteries for the duration of 3 hours. The arterial pressure in the carotid and the femoral arteries, renal volume, diuresis, and respiration were recorded during this period. It was found that no appreciable changes were caused by the occlusion. The pressure in the carotid artery was slightly elevated, the pressure in the femoral artery dropped abruptly to about 25 mm. of mercury, but never to zero. Severing of the femoral artery during the interruption of the aortic circulation produced considerable hemorrhage. No evidence of medullary lesions was found in any of the cases. The only damage caused by the relative ischemia was minor transitory lesions of degenerative character in the thigh muscles, and regeneration of the damaged tissue set in after the third day.

In a second group of 20 dogs a graft of the bifurcation was performed. The material for the graft was taken from other animals and consisted of the terminal aorta with its five branches, namely, two external iliac, and two hypogastric arteries, and the middle sacral artery. The specimens were about 5 cm. long, and, after being freed of the adventitia, they were put in a preserving solution. Only relatively fresh specimens were used; none was older than 39 days. The actual grafting operation is described in detail. It was done under pentothal sodium and intratracheal ether anesthesia and required from 2½ to 3½ hours.

In 13 of the 20 animals the operation was successful. The surviving animals were sacrificed after various periods (from 39 to 232 days after the operation), and the graft specimens were examined anatomically and histologically. In some cases the entire graft was calcified. Six of 20 dogs died from 2 to 14 days after the operation, 2 from hemorrhage, 1 from peritonitis, and 3 from other causes.

Although the author was able to show that successful substitution of the terminal aorta with its branches by graft is possible in dogs, it remains an open question whether this operation will ever be applicable to man. WERNER M. SOLMITZ, M.D.

BLOOD; TRANSFUSION

Circulating Anticoagulants in Hemophilia and in Hemophilialike Disease. KARL SINGER, ERNEST MOND, JULIAN HYMAN, and ROBERT C. LEVY. *Blood*, N. Y., 1950, 5: 1135.

Circulating anticoagulants have been found in patients with evident hemophilia and in those with hemophilia arising either anew or in association with various diseases showing signs and symptoms indistinguishable from hemophilia. In the first group of patients the circulating anticoagulant was considered as having developed as a result of immunization following blood transfusions and as probably being directed against the so-called "antihemophilic globulin," a plasma factor lacking in these hemophiliacs but supplied in the transfused blood. In the second group the circulating anticoagulants showed variations in their physiochemical properties and mode of action. This is the group to which the designation hemophilialike disease was applied.

The authors discuss 2 additional cases. One of the patients was of particular interest because his anticoagulant was dialyzable and remained demonstrable for a limited period only. The other patient had never been tested for the presence of a circulating anticoagulant, although it was assumed that he was a hemophiliac. The anticoagulant, however, showed up on the first examination in the laboratory.

Analysis of the mode of action of the anticoagulants in these 2 patients showed interference with the formation of thromboplastin, although some antithromboplastic activity could not be excluded.

The technique of analysis consists in drawing blood simultaneously by clean venipuncture with No. 20 needles from the patient and from a normal control. A stop watch is started at the first appearance of blood in the syringes; slight differences in time in obtaining the blood are insignificant in the presence of a potent anticoagulant. Three-tenths cubic centimeter of the patient's blood is put into each of three Lee-White clotting tubes previously marked at the 0.3 and 1.3 c.c. levels. One cubic centimeter of the normal blood is then added, each tube is inverted once and thereafter the clotting time is determined in the usual manner. The clotting time of the control subject is measured at the same time in an identical fashion, but 0.3 c.c. of normal saline solution is added to 1 c.c. of blood in each tube. The theoretic possibility exists that group incompatibility between the two tested bloods, with clumping, lysis, or both, of the red cells, may interfere with the test. However, this has not occurred.

Differentiation of these disorders is of practical significance because hemophilialike disease is not hereditary and the clotting anomaly may disappear spontaneously. STEPHEN A. ZIEMAN, M.D.

The Prevention of Thromboembolism. L. LOEWE, L. BERGER, R. P. LASSER. *Angiology*, 1951, 2: 26.

A program for the prevention of postoperative thromboembolic complications has been used at the

Jewish Hospital of Brooklyn, New York. Essential features include the administration of a single dose of repository heparin combined with free active movement and early ambulation. The recommended dose of heparin is 200 mgm., which produces a slight elevation of the blood coagulation time in 90 per cent of individuals.

One hundred and two patients, constituting a trial group, were subjected to this program and among these, 8 cases of thrombophlebitis and 1 case of nonfatal pulmonary embolism occurred. In a similar sized control group there were 11 cases of thrombophlebitis, 7 cases of pulmonary emboli, and 1 case of fatal pulmonary embolism. One patient died from hemorrhage following heparinization on the first postoperative day. Subsequent experience indicated that the 300 mgm. dose which this patient received was too large.

If early ambulation is not practical, as may be the case in colostomy patients with colostomies or certain orthopedic cases, repeated doses of repository heparin should be given every second or third day. If there is any suspicion of postoperative oozing, prophylactic anticoagulant therapy must be withheld until the third or fourth postoperative day.

In a recent group of 92 patients subjected to this program there were no thromboembolic complications, but of a similar unprotected group, 9 developed thromboembolic disease (9.6 per cent).

Ambulatory anticoagulant therapy with 100 to 300 mgm. of repository heparin administered at weekly intervals is practical for patients with chronic or recurring thromboembolic disease, and may be given without laboratory control. The object of this therapy is not to achieve prolongation of the coagulation time, but to correct the tendency toward hypercoaguability which might be responsible for intravascular clotting. A series of 20 patients have been treated in this manner for 18 to 56 months.

FREDERICK W. PRESTON, M.D.

LYMPH GLANDS AND LYMPHATIC VESSELS

Discussion on the Treatment of Chronic Edema of the Leg. SIR ARCHIBALD MCINDOE, A. M. BOYD, IAN AIRD, SIR HAROLD GILLIES, and OTHERS. *Proc. R. Soc. M.*, Lond., 1950, 43: 1043.

A symposium on the present status of the treatment of chronic edema of the legs is presented by the authors with a classification of the various types of edema. The chronic lymphedema still continues to resist surgical cure and in its treatment is most disappointing to the surgeon. The objects of the surgical treatment are:

1. To drain the lymphatic fluid into other channels peripherally, thus reversing the lymph flow. Various attempts have been devised to create an anastomosis between the superficial and deep lymphatics. The most common procedure, the Kondoleon operation, has not been very satisfactory.

2. To bypass the central obstruction of the lymphatics by bridging the skin from the arm to the leg or from one arm to the other; the skin is inserted in such a way that one end lies in the edematous tissue of the affected limb and the other is projected into the nearest available lymph drainage area. The operation is so lengthy and difficult that it should not be performed by other than plastic surgeons with a knowledge of flap transfer.

3. To remove the lymph-bearing area totally by replacing the limb with free skin grafts after the excision of all the subcutaneous tissue. The results in these cases have been very impressive and the method deserves further trial. The grafts act as a strong elastic stocking, preventing the accumulation of further fluid.

It is hoped that the inflammatory process originally responsible for the edema can be brought under control medically and cured in the earlier stages, as other inflammations, so that chronic lymphedema may become a rarity. These plastic surgical considerations in the treatment of chronic edema of the legs were presented by Sir ARCHIBALD MCINDOE.

A. M. BOYD presented his investigations on chronic edema of the legs and concluded that in all types of edema there is an early reversible stage during which the condition can be cured or held in check. The principles of the treatment at this stage are mobilization of the fluid, prevention of the accumulation of fluid in the dependent limb, and removal of the causative factor, if known.

Management during the reversible stage depends on the results of the careful investigation of the etiologic factors involved. The preliminary treatment consists of bed rest with the legs elevated on a wedged mattress. The degree of subsidence demonstrates the extent of permanent damage: when there is rapid and total disappearance of the fluid on elevation, complete cure should be possible; however, when reduction is incomplete, resolution may still take place over a period of time after correction of the circulatory defect. Before any logical treatment is possible, an assessment of the arterial and venous circulation is imperative. The only available method of correcting deep venous stasis is ligation of the main vein, whereby the column of blood is interrupted. The optimum site of ligation is still a matter of discussion; phlebography often shows the site and extent of the lesion and the degree of competence of the principal valves. Phlebographic findings are confirmed by the change in venous pressures on exercise. The main consideration of the site of the ligature should be the state of the valves, ligation being carried out at the level of the highest incompetent valve. Generally, this implies ligation of the superficial femoral vein in old cases of iliofemoral thrombosis, and of the popliteal vein in deep phlebitis of the calf which has extended proximally to destroy the popliteal valve. Lumbar ganglionectomy is valuable only when the symptoms of deep phlebitis are due to vasospasm which interferes with arterial inflow and restricts the collateral channels.

The management of the irreversible stage characterized by the thickening of the deep fascia and

fibrosis of the subcutaneous tissues as a result of persistent edema must be directed to the prevention of further deterioration by the use of elastic compression and by careful avoidance of all types of infection of the skin because the condition may lead to recurrent cellulitis followed by lymphatic obstruction. A modified Kondoleon operation is indicated when the limb becomes heavy and painful, the wearing of shoes is impossible, and ulceration of the skin is imminent.

IAN AIRD in his discussion points out the importance of controlling the edema while it is still of a pitting kind. An elastic bandage and, preferably, bed rest initially, with the use of elastic stockings later, will aid in controlling the edema. The elastic stocking should extend to the groin and be supported by a belt. The stocking is continued in posttraumatic and postthrombotic cases for a year or so, in angioneurotic and inflammatory cases for as long as attacks occur, and in other cases for life. Solid edema can be relieved by operation. The aim of the operation is to remove the fluid in the extracellular space of the subcutaneous tissues. It may often be necessary to place skin grafts on the underlying muscle after the excision of the atrophic skin with the subcutaneous tissues as indicated by Sir Archibald McIndoe.

The "lymphatic wick" procedure is a radical cure in chronic lymphoid edema and has been used in cases in which there is a definite block in the iliac region of the lymphatic vessels. The bridging of the block is done with elevating flaps from the arm, embedding them into the abdominal wall, and stretching them from below Poupart's ligament to the lower limb. Thus, the thigh is drained through the new lymphatics into the lower part of the axillary lymphatic drainage. This procedure has a limited application and further research must be done along the lines of the "lymphatic wick."

A. J. WALKER presented a method of determining the venous pressure and of phlebography for the diagnosis of swollen legs of venous origin. It was his conclusion that ligation of the main vein must not be done in patients with edema, eczema, or ulcer, in whom the venous pressure is not lowered by exercise with a light tourniquet below the knee. If the main vein is patent and incompetent, as shown by the pressure readings, he advocates ligation of the popliteal vein.

RATCLIFFE analyzed the serum and tissue fluids from edematous limbs and found the results to be normal. The only positive finding was that the albumin-globulin ratio was either high or the same as in the serum.

S. S. ROSE studied the problem of edematous legs with x-rays. He found that a typical pattern can be observed in the soft tissues, this pattern being dependent on the increase in the thickness of the fibrous tissue, septa, and fascia. The edemas of recent origin, for example, those starting within the last 2 years, are found to reveal a fine bubbly appearance; and in later years a much coarser, wider-meshed network with fibrous trabeculation is found in the soft tissues. A further point of distinction arises in the comparison of venous and so-called lymphatic edemas. Apart from the comparative lack of mottling in the venous edema, the swelling is distributed evenly through the whole leg, as opposed to the gross swelling outward from the deep fascia in the "lymphatic" type.

JOHN E. KARABIN, M.D.

SURGICAL TECHNIQUE

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Deaths from Dicumarol. LOUIS T. WRIGHT and MILTON ROTHMAN. *Arch. Surg.*, 1951, 62: 23.

The authors summarize the causes of death in 32 cases of hemorrhagic diathesis ascribed to dicumarol which were found in the literature and add 4 fatalities of their own which occurred in a series of 136 patients treated with dicumarol at the Harlem Hospital, New York City. Review of the literature revealed that the majority of the fatalities were caused by gross overdosage of dicumarol. The lack of uniformity of the prothrombin determinations led to poor anticoagulant control, but even patients with from 20 to 30 per cent prothrombin activity and pre-existing phlebothrombosis developed repeated pulmonary infarctions and even fatal pulmonary emboli. The authors tend to accept Ochsner and Kay's hypothesis that intravascular clotting is determined by the relative disproportion between the prothrombin and the antithrombin levels of the blood, and that when this disproportion becomes great enough, thrombo-embolic disease occurs. This theory would explain the appearance of thrombi and emboli in patients with markedly depressed prothrombin activity, and would lend support to the thesis of Arthur Allen that bilateral superficial femoral vein interruption is a safe and adequate method of preventing thrombosis and embolism.

Three of the 4 cases reported in detail presented normal prothrombin levels before dicumarol therapy, but 1 patient's control prothrombin time represented only 60 per cent of the normal prothrombin activity. Daily prothrombin determinations were made, and all patients were held in a range between 30 and 40 per cent prothrombin activity. Despite apparently adequate control of the dicumarol dosage, all 4 patients developed hemorrhagic diatheses and expired despite strenuous therapy with whole blood and Vitamin K. No potassium oxide was used. The authors conclude that probably their prothrombin time determinations were at fault.

MALCOLM PLUM, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Early Care of the Seriously Wounded Man. HENRY K. BEECHER. *J. Am. M. Ass.*, 1951, 145: 193.

Paramount among the general considerations of the early care of the seriously wounded man are speed in forward evacuation and early preparation for surgery. Proper timing of the surgical intervention is most important, and although the shock phase following wounding may still be present when surgery is started, it is possible to induce anesthesia on the tide of a rising blood pressure by the use of whole blood and oxygen before induction. Some patients with penetrating abdominal wounds will fail to respond to adequate amounts of whole blood, and these men will usually have continued concealed hemorrhage or widespread peritoneal contamination.

In field care prior to hospital admission, priority is given to establishing a clear airway, the application of splints and tourniquets, control of hemorrhage, closure of sucking chest wounds, and the administration of plasma, morphine, and tetanus toxoid. Artificial respiration should not be overlooked, if needed. Tourniquets should be applied to control hemorrhage and should be loosened at half-hour intervals if arterial pressure is satisfactory, in order to maintain nutrition to the limb distal to the tourniquet and prevent complete venostasis. When a limb is hopelessly mangled, a tourniquet is applied just below the site of election for amputation and left in place.

Specific preoperative procedures include a complete physical examination of the patient with all clothing removed. The intravenous administration of 10 mgm. of morphine is the medication of choice for pain, but much can be accomplished with sodium nembutal or amytal given intravenously to allay anxiety. Gastric aspiration is usually essential before anesthesia; oxygen therapy is indicated in thoracic injuries or in the presence of shock, cyanosis, tachycardia, or depressed respiratory exchange. Whole blood is essential to the patient who has suffered blood loss, whether or not he is approaching shock. If the patient fails to respond to intravenous transfusion, from 200 to 300 c.c. of blood injected into the radial artery may rapidly restore the systolic blood pressure. Three hours is the maximum time allowed for the preparation of even the most seriously wounded patient for surgery, for further delay usually indicates improper organization of care.

The early care of men with specific types of wounds is outlined. In treating maxillofacial injuries, no hesitation should accompany the performance of a tracheotomy for an obstructed airway. Patients with maxillofacial injuries are evacuated in the prone position. Men with penetrating eye wounds should have both eyes bandaged and should be evacuated in the sitting position to prevent escape of the vitreous. In the treatment of thoracic wounds, tight occlusion of open chest wounds with gauze and adhesive strapping is of prime importance. Tension pneumothorax with a shifting mediastinum and cardiac irregularities should be constantly watched for; a chest tap with relief of positive pressure may be life-saving. A catheter inserted through a trocar and sealed with a flutter valve or water seal is the best temporary treatment of a bronchopleural fistula. Oxygen, blood, and the relief of chest pain to produce more effective raising of secretions are of obvious importance.

Patients with penetrating abdominal wounds should receive high priority in evacuation. Transfusion, gastric aspiration, and the relief of pain are essential. Patients suffering from frost-bite are treated with gradual restoration of heat, antibiotics, prevention of maceration, and anticoagulants. Gas gangrene is one of the feared complications of long uncared-for wounds with great tissue loss, soil contamination, or arterial occlusion. Thorough débridement, transfusion, antibiotics, and polyvalent antiserum are essential. Compound fractures are often accompanied by great blood loss, and the patient must receive whole blood as well as speedy evacuation. Early treatment of severely burned patients consists in the intravenous administration of plasma and sodium chloride in addition to a mixture of sodium chloride and sodium bicarbonate given by mouth. Morphine should be given intravenously for pain. General anesthesia should be avoided in the recently burned patient, and pentothal sodium is absolutely contraindicated.

In the relief of pain, the intravenous administration of 10 mgm. of morphine is the medication of choice, but morphine should not be used routinely on all wounded men—only when severe pain is present; otherwise aspirin, codeine, or a barbiturate should be used to relieve anxiety. Seriously wounded patients are abnormally sensitive to morphine. Morphine should not be given to the "walking wounded," to patients with liver disease, head wounds, chest wounds when the respiration is already impaired, or those with shock unless severe pain is present. Morphine poisoning usually occurs from several subcutaneous doses which are not absorbed until the local circulation is restored with adequate shock treatment. Treatment of morphine poisoning consists in applying a tourniquet proximal to the injection site, and in giving oxygen and artificial respiration, if necessary. One milligram of atropine (intravenously) may be of value, and 30 mgm. of ephedrine (intravenously) will support a falling blood pressure. Frequent change in position is desirable.

In the choice of anesthesia for seriously wounded men, nitrous oxide ranks high for short term anesthetics. Ether given endotracheally is the agent of choice for prolonged procedures after emptying of the stomach. Local anesthesia is seldom of value. Spinal anesthesia should be avoided in the seriously wounded. Pentothal sodium is far too freely used in the seriously wounded because of its ease of administration, speed and ease of induction, and the rapid recovery of the patient. Pentothal sodium is a dangerous drug in the seriously wounded and should be given only in a 2.5 per cent solution with the routine administration of oxygen in all anesthesias lasting more than 30 minutes. It is contraindicated in morphine overdosage, when shock is present or anticipated, and when a cervical abscess is to be drained. Patients undergoing intracranial operations or treatment for severe burns tolerate pentothal sodium anesthesia poorly. It is most valuable in providing anesthesia for short procedures when no relaxation is needed in patients in relatively good condition. MALCOLM PLUM, M.D.

Physiological Reaction to Pituitary Adrenocorticotropic Hormone (ACTH) in Severe Burns. M. JAMES WHITELAW. *J. Am. M. Ass.*, 1951, 145: 85.

Treatment of 1 severely burned patient with ACTH alone is reported in detail. A previously healthy 23 year old white male suffered 70 per cent second and third degree burns from gasoline; he was immediately hospitalized and during the first 24 hour period received 9,000 c.c. of plasma, 2,000 c.c. of dextrose in saline solution, and, in addition, consumed some 5,000 c.c. of fluid orally. Pressure dressings were applied and penicillin was administered.

At the end of the first 24 hour period he was transferred to another hospital where the only treatment consisted in the administration of ACTH (20 mgm. every 6 hours) plus ascorbic acid (1 gm. per day). A direct phloxine eosinophil count before the institution of treatment showed complete disappearance of circulating eosinophils. After ACTH therapy had been started, pain became less pronounced and fever rapidly subsided. Oozing subsided to such an extent that there was no evidence of active oozing on the fifth day when the dressings were changed. Fluid intake by mouth was excellent, and by the fifth day the patient was consuming 3,000 calories daily including 100 gm. of protein. The urinary output steadily increased and exceeded 8,000 c.c. on the sixth hospital day. At this time a right lower lobe pneumonia developed which was treated successfully with aureomycin. The dosage of ACTH was increased to 25 mgm. every 6 hours from the tenth to the eighteenth hospital day, when the dosage was cut to 10 mgm. every 6 hours. Epithelization of the second degree burned areas proceeded apace without fibrosis. On the forty-second hospital day, homologous pinch grafts from 2 donors were applied to the third degree burned areas; 97 per cent of these pinch grafts took rapidly, and epithelization around them proceeded at a very rapid rate. Total re-epithelization was complete 2 months following the pinch grafting.

The author emphasizes the economy of material, money, and professional time effected by ACTH, as well as the survival of a severely burned individual whose prognosis with the conventional forms of treatment would have been doubtful. Adequate stimulation of a normal adrenal cortex apparently eliminates or greatly reduces the physiological phenomena usually accompanying severe thermal burns. MALCOLM PLUM, M.D.

Mortality in Patients with Burns (Mortalidad por quemaduras). GUSTAVO LABRA EDWARDSON-MEEKS. *Prensa méd. argent.*, 1950, 37: 2944.

The author presents a statistical analysis of the morbidity and mortality due to burns, as recorded in the hospitals of Chile, during the period from 1920 to

1947. Although the morbidity has increased significantly since 1920, the mortality rate shows a definite decrease.

The steady increase of patients in hospitals in the past three decades, who are suffering from wounds due to burns and other causes, is due to several factors. These are: (1) a general increase in the population, from 3,753,799 in 1920 to 5,574,175 in 1947; (2) development of new industries, in which the production involves the application of thermal, chemical, electrical, and other burn-causing agents; (3) engagement of more workers in the factories; and (4) a more generalized acceptance of hospital care by the population.

In a previous article the author discussed the fundamental principles which should be observed in the treatment of burns. He emphasizes the importance of the prevention, recognition, and early treatment of complications. Strict asepsis, adequate care of the wound, the prevention or the relief of shock, control of infection, correction of anemia, and maintenance of nutrition are the most important points of therapy. Administration of blood plasma as the best method for a controlled replacement therapy and systemic use of antibiotics are, in the author's opinion, the main causes for decrease of the mortality rate in burns since 1920. OLGA M. HARING, M.D.

Local Treatment of Suppurative Lesions of the Hand with Penicillin (Lokale Penicillinbehandlung eitriger Erkrankungen der Hand). D. FOGARASI. *Wien. med. Wschr.*, 1950, 100: 809.

If the patient comes for treatment within 8 hours after the injury, the author sutures his wound after débridement and injects into the surrounding tissues from 1 to 2 c.c. of penicillin solution containing 20,000 units per cubic centimeter. If the injury dates further back, the treatment consists of a similar injection and application of an ointment containing sulfonamides.

Early stages of felons, phlegmons of the palm, furuncles, and carbuncles are treated with daily local injections of from 20,000 to 40,000 units of penicillin on 3 or 4 successive days. The involved hand is immobilized, and, in the majority of patients, inflammatory process usually recedes.

In more advanced conditions the same amount of penicillin is injected locally, and the pus is evacuated by puncture or small incision. Counterincision and drainage are superfluous. The injections are repeated daily until suppuration subsides. The affected extremity is immobilized.

If lymphangitis and lymphadenitis are present and do not yield to the first penicillin injection, additional injections of 20,000 units each are given in 2 or 3 places along the course of the inflamed lymph vessels. When the secretion begins to subside and the necrotic tissue has been expelled, hot baths and active exercises are prescribed to prevent stiffness of the articulations, and atrophy due to inactivity.

In 204 patients, of 804 with felons or phlegmons, incision preceded penicillin injections, while in 600 patients either the antibiotic alone was employed or the injection was followed by a small incision.

Inflammatory processes of tendon sheaths also responded well to this therapeutic method. The affected sheath was exposed but not incised and 40,000 units of penicillin were injected into it on 3 or 4 successive days. The involved extremity was immobilized.

The author highly recommends this combined antibiotic and surgical treatment.

JOSEPH K. NARAT, M.D.

ANESTHESIA

Sudden Death Occurring Immediately After Operation in Patients with Cardiac Disease, with Particular Reference to the Role of Aspiration Through the Endotracheal Tube and Extubation. HARRIS B. SHUMACKER, JR., and L. JENNINGS HAMPTON. *J. Thorac. Surg.*, 1951, 21: 48.

Sudden death at the termination of surgery during aspiration through an endotracheal tube or on extubation might occur by effecting a transient state of decreased oxygen saturation with a resulting increase in susceptibility to vagovagal reflex causing a cardiac arrest. In addition, a relative state of hypoxia existing previous to surgery could bring this mechanism into play with greater ease.

The authors present 5 patients with known cardiac disease dying suddenly following aspiration through the endotracheal tube or on extubation at the termination of the operation. Four of these patients had congenital heart disease and 1 had auricular fibrillation and myocardial damage from an unknown cause. In each the operation and anesthesia had proceeded satisfactorily, and in each cardiac massage and stimulation shortly following arrest was to no avail.

Earlier work by others had demonstrated that an electrocardiographic change occurred on stimulation of the tracheobronchial tree by an aspirator or endotracheal tube; that an abrupt drop in oxygen saturation did occur during these procedures; and that unless oxygen was administered under pressure, several minutes were required for a return to the pre-existing level of oxygen.

It is suggested that perhaps such cardiac arrests could be prevented by expediting aspiration and extubation to prevent undue decrease in oxygen saturation, by inflating the lungs with 100 per cent oxygen previous to this procedure, and by the administration of atropine near the completion of the operation before endotracheal manipulation is performed. HERBERT J. KAROL, M.D.

Neuropsychiatric Sequelae of Cardiac Arrest During Spinal Anesthesia; One Year Follow-up of a Case. V. A. KRAL. *Canad. M. Ass. J.*, 1951, 64: 138.

An 18 year old boy suffered cardiac arrest while undergoing an inguinal herniorrhaphy under spinal anesthesia obtained with pontocaine hydrochloride

in glucose. The arrest was terminated by cardiac massage and intracardiac procaine injection, after a period estimated to be 4½ minutes. A state of decerebrate rigidity developed which lasted for 48 hours. This was followed by a decorticate state lasting for about 4 weeks and which was interrupted by attacks of complete decerebration.

Three months after the arrest occurred there were signs pointing to involvement of the basal ganglia, cerebellum, the cervical part of the spinal cord, pyramidal tract, and the sleep-regulating apparatus in the diencephalon. Severe cortical damage was reflected in the psychiatric symptoms. In the following months the signs referable to the damage of the spinal cord and the lower parts of the brain improved steadily and eventually subsided completely. The symptoms indicating cortical damage, on the other hand, showed improvement during the first 7 months after circulatory arrest occurred, after which time they remained practically unchanged. The patient was followed up for a year.

The observations of the author seem to bear out the pathological findings in man and experimental animals that in stagnation and anoxic anoxia the cerebral cortex is subject to the most severe and extensive damage. The cerebellum, basal ganglia, and lower part of the brain stem are less vulnerable to anoxia. The anatomical changes found in these regions are less severe and more easily reversible. The author's case as well as experiments have shown that the anterior horn cells of the spinal cord are vulnerable to anoxia, but capable of physiological and histological restitution even after long periods of exposure to anoxia.

The cause of the cardiac arrest during spinal anesthesia could not be determined.

JACOB T. BRADSHER, JR., M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Repair of Large Radiation Ulcers Situated Over the Heart and the Brain. JOHN MARQUIS CONVERSE, ROSS M. CAMPBELL, and WILLIAM L. WATSON. *Ann. Surg.*, 1951, 133: 95.

Because of the peculiar destructive effect of radiation on all tissues, reconstructive surgery often must meet unusual and difficult problems. It is necessary to excise not only the ulcerated area, but all of the immediate adjacent tissues of even the least unhealthy appearance. In order to accomplish this it is necessary at times to transplant healthy tissues from areas of considerable distance from the ulcers. The authors report 2 cases.

In the first case the ulcer extended over the chest and the defect exposed the pericardium. A flap was taken from the right abdominal wall and was transplanted first to the right forearm. It was then mobilized over the chest defect. The take was excellent and the reconstruction in the illustration gave the appearance of a normal breast.

In the second case the defect extended over the entire frontal area. After débridement a similar transplantation procedure was performed with use of the skin of the upper left abdominal wall; it was attached to the left forearm, and the flap then was transplanted to the cranial defect. The final results were devoid of any grotesque disfiguration.

STEPHEN A. ZIEMAN, M.D.

Complications of Decubitus Ulcers in Patients with Paraplegia. HERBERT CONWAY, RICHARD B. STARK, JOHN C. WEETER, F. A. GARCIA, and J. D. KAVANAUGH. *Plastic & Reconstr. Surg.*, 1951, 7: 117.

Experience with 102 decubiti in patients with paraplegia has attested to the soundness of surgical technique, which includes the following steps: (1) complete excision of the ulcer and regional scar tissue, (2) excision of regional new bone formation, together with the underlying bony prominence, (3) rotation of a flap of muscle over the exposed bone, (4) closure of the wound by the use of a flap of skin and fat rotated to the area of the decubitus, placed so that suture lines and resultant scars are not over the site of the previous decubitus, and (5) the use of a free graft of skin at the point from which the flap was elevated.

The excision of the underlying bony prominence has resulted in an increased percentage of success in the operative closure of decubiti. As patients leave the bed for a wheel chair existence, an increase in the occurrence of decubiti over the ischial tuberosities is found. Excision of the underlying bony prominence has effected a dramatic improvement in the results of operative treatment in such cases. When this step was not employed, healing was maintained in only 47 per cent of cases; after its use, healing was maintained in 80 per cent of cases.

SAMUEL KAHN, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Experimental Neurography. I. M. TARLOV, DOREEN BERMAN, and JOSEPH EPSTEIN. *Am. J. Roentg.*, 1950, 64: 974.

The authors have performed numerous experiments on rabbits with the purpose of finding an innocuous opaque medium for the roentgen visualization of a peripheral nerve or nerve root. In particular, they have studied the functional and histopathologic effects as well as the qualitative value of the opaque media in providing good delineation of the nerves for use in clinical neurography.

A review of the literature revealed that such attempts have been made periodically since 1928, and that a series of contrast agents have already been tested. These included collargol, colloidal compound of silver, various compounds of lead, mercury and iodine, lipiodol, jodipin (Merck), pantopaque, an emulsion of iodized oil and honey called l'ombre, thorotrast, perabrodil, etc. Most investigators employed thorotrast for clinical application despite its radioactive effect over an extended period.

The authors investigated the various radiopaque compounds by injecting them into the sciatic nerve which was exposed under open-drip ether or intravenous nembutal anesthesia. The nerve, after being cleared of its enveloping fascia, was carefully elevated by means of a blunt nerve hook and the contrast medium was injected under slight digital pressure. The injection usually was made at a point midway between the head of the great trochanter and the popliteal fossa. The opposite limb of the rabbit was injected with saline solution or air, for control. Roentgenograms were taken and functional studies were made immediately after the injection and at certain intervals thereafter. In most cases the rabbits were not sacrificed until they showed full functional recovery as well as absorption of the injected material. The histopathologic study of the sciatic nerve was carried out in minute detail.

The following radiopaque substances were tested:

Water soluble compounds: (1) argyrol in 50 per cent solution; (2) protargol in 15 per cent solution; (3) hippuran in 50 per cent solution; (4) skiodan, in 100, 75, and 50 per cent solutions; (5) thorotrast, in 25, 12.5, and 6.25 per cent concentrations; (6) sodium iodide, in 100, 50, 25, 20, 15, and 10 per cent solutions; (7) neoiopax, in 50 and 25 per cent solutions; (8) diodrast, in 70, 35, and 17.5 per cent solutions; (9) 6-iodo-d-galactose in 40, 20 and 13.3 per cent concentrations; (10) viscorayopake in 35, 23.5, and 17.5 per cent solutions.

Water insoluble compounds: (1) iodochloral; (2) lipiodol; (3) diiodotyrosine in 25 per cent suspension; (4) pantopaque in original form and in forms chemically emulsified with Tween 20, Tween 80, and Yelkin BSS.

The results obtained with the above enumerated substances are described in detail. Several reproductions of neurograms and photomicrographs are included to illustrate the roentgen delineation of the sciatic nerve and the structural changes produced.

The following conclusions were reached:

1. All of the compounds included under water soluble compounds, with the exception of thorotrast, either gave unsatisfactory neurograms or, when the roentgen visualization was satisfactory, produced marked toxic effects functionally and structurally on the sciatic nerve.

2. Thorotrast proved to be a good radiopaque agent but in view of its known late harmful effects, due to radioactivity, its use for clinical neurography is not recommended.

3. Of the compounds included under water insoluble compounds, lipiodol and pantopaque gave very good delineation of the sciatic nerve. The lipiodol, however, is too viscous for intraepineurial injection and, moreover, it had some untoward side effects.

4. The pantopaque, when used in the original form, in amounts of 0.2 c.c., produced either no functional and histopathologic changes, or minimal ones. With larger quantities, however, serious functional and histopathologic alterations occurred. Likewise, the use of the aforementioned emulsified forms of pantopaque resulted in markedly deleterious functional and histopathologic effects on the sciatic nerve.

5. Although unaltered pantopaque used in small quantities appears to be a satisfactory contrast medium for clinical neurography, the authors believe that it cannot yet qualify for routine diagnostic application and that the search for a more suitable substance should go on. T. LEUCUTIA, M.D.

Evaluation of Aortography in Abdominal Diagnosis. L. R. SANTE. *Radiology*, 1951, 56: 183.

A quarter of a century has elapsed since dos Santos and his associates began their work on injection of the circulation with contrast material to render the vascular structures opaque on x-ray examination. Much of the roentgenographic material presented is from the examination of over 3,000 cases reported by Melick and Vitt, and by Hartnett. The modified Wagner method is used and advocated at present.

Contraindications are similar to those holding for injection of the same materials into the circulation in other procedures, such as intravenous urography, arteriography, cardioangiography, etc. Among those which have been mentioned are: advanced renal destruction with uremia, severe disease of the liver, exudative diathesis, severe hyperthyroidism, advanced tuberculosis, and iodine sensitivity.

Aortography provides a demonstration of the blood supply to abdominal organs and evaluation of its quantity, character, and distribution. It is evident that variation from the normal vascular pattern is the means by which various pathological conditions can be recognized. Variation in the size of the vessels supplying an organ becomes a matter of judgment. Supernumerary vessels, however, can usually be readily detected and appraised. Variations in distribution of the arterial supply to some part of an organ may signify a structural change, such as a cyst, neoplasm, or parenchymal destruction; avascularization may mean necrosis or atrophy from chronic pressure from a large hydronephrosis. Large solitary cysts of the kidney show a decrease in vascular supply with fine scanty vascular structures widely divergent over the surface of the expanding cyst, since the blood vessels are in the capsule, and not in the center of the tumor. Neoplasms of the kidney, on the other hand, due to their extreme vascularity may show "puddling" or "laking" of the circulation within the tumor, which is quite characteristic when encountered. This appearance of "puddling" of the circulation may not be evident immediately but may be seen on later films as the larger vessels have been swept clear and the retarded material in the tumor is detected. An extreme example of puddling is seen in the placenta. In the detection of placenta previa, this is a most helpful method. Actual cortical necrosis from any cause will show complete avascularity of the area involved. Pressure atrophy of the entire kidney parenchyma from a large hydronephrosis may cause almost complete avascularization of the kidney. Pressure of the enormously distended pelvic structure upon the circulation may result in cutting off of the primary blood supply.

All of the conditions mentioned produce large rounded masses involving the kidney structure. It is obvious, then, that aortography may be a great aid in differentiation. By demonstrating the quantity, character, and distribution of the blood supply to abdominal organs, this procedure makes possible the recognition and differentiation of various pathological conditions, notably renal cysts and neoplasms, placenta previa, and ischemia of the renal circulation. In the presence of renal anomalies and hydronephrosis, aortography, by demonstrating the adequacy of the blood supply, furnishes a valuable guide to treatment. FRANK L. HUSSEY, M.D.

Primary Reticulocell Sarcoma of Bone; Summary of 37 Cases. BRADLEY L. COLEY, NORMAN L. HIGINBOTHAM, and HARVEY P. GROESBECK. *Radiology*, 1950, 55: 641.

Thirty-seven cases of primary reticulocell bone sarcoma from Memorial Hospital (New York), are reviewed. The authors use the following criteria for inclusion: (1) clinically, a primary focus in a single bone on admission; (2) unequivocal histologic proof from the bone lesion; (3) metastases present on admission only if regional, or if the onset of symptoms of the primary tumor preceded the appearance of metastases by 6 months.

The tumor may occur at any age, but its greatest incidence is in the second and third decades; 70 per cent of patients are under 40 years of age. In 65 per cent of cases in this series the lesions occurred in the long bones. Fifty per cent were in the lower extremities.

The symptoms observed were those of any primary bone tumor: pain, swelling, and disability. Pain was the most significant symptom, usually being the first indication, and was present in all cases on admission. It was typically intermittent at first, becoming constant with increase in size of the tumor, or with pathologic fracture. Although frequently localized to the site of the tumors, pain was referred to the nearest joint in 70 per cent of the cases.

The treatment of choice is believed to be radiation therapy and the authors deliver a dose of 3,000 to 4,000 roentgens to the tumor. The lesions were found to be not only highly radiosensitive, but also highly radiocurable. Exclusion of those cases which were treated for palliation only, showed a 5 year survival of 73 per cent of patients and a 10 year survival rate of 55 per cent. Although metastases and recurrence may occur after a period of 10 years or more, many of these may be controlled further by radiation or surgery.

The article includes a detailed discussion of the pathological, clinical, and radiological findings.

JOHN WEIGEN, M.D.

The Development of Periosteal Knee Joint Shadows in Paraplegics (Ueber das gehaeufte Vorkommen parostaler Knochenneubildungen bei Querschnittsgelaehmten). H. LUEDEKE. *Fortsch. Roentgenstrahl.*, 1950, 73: 564.

The author presents an excellent review of the literature concerning a lesion first described by Pellegrini in 1905, and later by Stieda in 1908. The lesion is a para-articular callus and neo-osseous formation noted in young people following trauma. The author points out the fact that this is very common in paraplegics, particularly those with transverse myelitis or cerebral injury.

In a group of 38 patients with transverse myelitis, the author found 12 cases of dense calcification at the medial aspect of the distal end of the femur, and 9 cases of ossification about the hip joint. Anatomically the lesion tends to develop slightly above the anterior aspect of the medial femoral condyle. Histologically and anatomically this process of ossification of the periosteum in paraplegics is identical to Pellegrini-Stieda's disease.

The mechanism of formation suggested in these cases is that spasmodic bending of the knee, such as that seen in patients with transverse myelitis, may cause tissue laceration or trauma, with subsequent ossification of the periosteum as a repair process. Thus, this process in paraplegics may be similar to the trauma-induced lesion in normal young adults.

JANE C. MACMILLAN, M.D.

Fig. 1a Fig. 1b

Fig. 3
(Simonetti and Tomiselli)

Direct Aneurysmography (Aneurismografia diretta). C. SIMONETTI and M. TOMISELLI. *Radiol. med.*, Milano, 1950, 36: 1013.

In direct aneurysmography, a lumbar puncture needle is introduced into the suspected aneurysmal sac. The needle, by means of a two-way connection, can be attached to a manometer and to a 20 c.c. syringe containing a citrate solution.

The pressure of the blood in the aneurysm and the type of the bloody jet into the syringe after citrate injection gives information as to whether the aneurysm consists of an enlarged canal or a saccular cyst. This is of importance to the surgeon in deciding the procedure to be employed in treatment.

After an injection of citrate into the supposed aneurysm, the syringe is changed and from a second syringe 20 c.c. of a contrast medium are injected over a period of 1 to 2 seconds.

The first roentgenogram is taken after the introduction of the first 10 c.c. of contrast solution, and another during the injection of the second 10 c.c. A third roentgenogram is then taken after the injection has been completed. The same type of exposure is made as that used in cerebral arteriography with a distance of 1 meter, from 70 to 75 kv., and an exposure of 1/10 second.

Figure 1a shows a patient with an aneurysm of the right subclavian artery and 1b shows a roentgenogram of the aneurysm after a direct injection of contrast medium into the aneurysm. The patient was treated by ligation of the subclavian artery below the internal mammary artery and ligation of the axillary artery above the subscapular artery.

Fig. 2a Fig. 2b

Figure 2a shows a patient with an aneurysm of the left axillary artery and 2b shows a roentgenogram of the aneurysm after a direct injection of contrast medium into the aneurysmal sac. In this case the manometer indicated a pressure of 60 mm. of mercury and only 10 c.c. of contrast medium had been injected. The aneurysm in this case was found to be a saccular one communicating with the axillary artery. The operation employed consisted of resection of the aneurysmal sac and suture of the axillary artery.

Figure 3 shows a roentgenogram of an aneurysm of the innominate artery. The patient presented a pulsating tumor at the right base of the neck, parallel and internal to the sternocleidomastoid muscle. It was the size of a pigeon's egg.

All 3 cases were syphilitic in origin.

In none of the cases were there signs of hemorrhage or rupture of the aneurysmal sac.

Direct aneurysmography is indicated in the study of suspected aneurysms of the peripheral arteries, especially those of the carotid, subclavian, axillary, brachial, and femoral arteries. It is not harmful to the patient. BLACKWELL MARKHAM, M.D.

Diagnosis and Treatment of Lymphoblastoma and Leucemia from the Standpoint of the Radiologist. JOSEPH L. MORTON. *Am. J. Roentg.*, 1950, 64: 919.

The present article is part of a symposium entitled "Combined Management of Hematologic and Allied Diseases from the Medical and Radiologic Viewpoints," presented at the Fiftieth Annual Meeting of the American Roentgen Ray Society, in October, 1949 at Cincinnati, Ohio. A plea is made for close co-operation between the internist, hematologist, pathologist, and radiologist in the management of cases of lymphoblastoma and leucemia. The radiologist has an important role both in the diagnosis and treatment of these diseases.

Lymphoblastoma and leucemia have in common their location in the recticuloendothelial system,

their unexplained fundamental etiology, and variable course to a fatal termination.

The diagnostic radiologist has the initial problem of determining, by means of a roentgenographic survey, the most efficient diagnostic approach, whether this should consist of aspiration biopsy, exploratory operation, or the use of other laboratory and clinical methods of differentiation. Diagnosis exclusively by biopsy may lead to error in several situations. Leucemoid reactions may be confused with myelogenous leucemia, and virus infections producing enlargement of the lymph nodes with or without lymphocytosis may lead to the faulty diagnosis of lymphatic leucemia or lymphoblastoma. In the presence of toxic depression of the bone marrow, roentgen study may be successful in locating tumors and infections.

The author condemns the so-called "therapeutic trial" by irradiation in mediastinal and abdominal tumors, since, with present advances in anesthesia and surgical techniques, the risk of performing thoracotomy or laparotomy for tissue biopsy is less than that of not knowing when or where to treat the disease.

Roentgenologic examination of the abdominal viscera by means of plain films, barium enema, and upper gastrointestinal series is particularly valuable for the location of intra-abdominal primary lymphoblastomas, as well as for the discovery of secondary extensions. Roentgenographic measurement of the spleen is fairly reliable in diagnosing enlargement of this organ. If the product of the horizontal and vertical dimensions exceeds 75 cm., a splenomegaly must be suspected. In rare instances, when the spleen lies downward and away from the diaphragm, examination of the patient in the erect position (with the stomach and colon filled with barium) is necessary to demonstrate the size of the spleen. Pneumoperitoneum is likewise a useful method but is not without discomfort and danger. Visualization of the liver and spleen by means of thorotrast is not recommended except in the very rare cases of congenital hemolytic icterus in which symptoms persist or recur after splenectomy.

The author also mentions several instances in which roentgen study of the affected area or of the adjacent regions, or even more distant parts of the body may help to establish a probable diagnosis which then must be confirmed by biopsy whenever possible. Such instances are: the demonstration of esophageal varices; a large spleen and a small liver in Banti's disease; the finding of the typical bone changes in Gaucher's disease; the visualization of engorgement manifestations of the lungs in polycythemia rubra, or of "potato nodes" of the mediastinum in Boeck's sarcoidosis, etc.

At times all available methods fail and diagnosis is established by deductive reasoning. This is especially true in extension of Hodgkin's disease to the para-aortic lymph nodes, the early enlargement of which is very difficult, if not impossible, to detect. The visualization of an early enlargement of the mediastinal lymph nodes may be enhanced by letting the patient blow into a mercury manometer while a roentgenogram of the chest is taken. Increase of the intra-alveolar pressure above 45 mm. of mercury will make the suspected nodes appear more prominent on the films.

The author deals only very briefly with the treatment of lymphoblastoma and leucemia. Localized lymphosarcomatous lesions are irradiated more intensively up to skin tolerance for the chosen portal area. In leucemia, daily doses of 50 to 100 roentgens are given, being guided by repeated blood counts so as not to over-treat. For nonleucemic lymphomas, including Hodgkin's disease and giant follicular lymph node hyperplasia, a dose of at least 2,000 roentgens is advocated to the tumor mass and contiguous lymphatics, by employing comparatively heavy filtration. T. LEUCUTIA, M.D.

The Treatment of Malignant Tumors of the Nasopharynx. SIMON KRAMER. *Proc. R. Soc. M.*, Lond., 1950, 43: 867.

Cancer of the nasopharynx is uncommon. The author presents a series of 54 cases observed at the Middlesex Hospital, London, between 1935 and 1949. Cancer of the nasopharynx occurs throughout the various age groups, and not infrequently in young subjects. In this series 8 patients were 30 years old or less, and 21 were 45 years or less. Men outnumbered the women at the rate of 36 to 18. The initial symptoms may be classified under three headings: rhino-otological symptoms, symptoms with extension beyond the nasopharynx with the usual tendency toward invasion of the base of the skull, and symptoms involving the enlarged lymph glands. In this series 26 patients first complained of enlarged lymph glands in the neck, and 41 enlarged cervical glands were detected at the first examination. Biopsy of the growth is most important both for histological verification and to determine the type of treatment to be given. It should be performed before treatment is started, as some of the growths are so radiosensitive that histological recognition may be very difficult after treatment. In this series biopsy was performed in 52 of 54 cases. In 47 cases it was positive, while no definite tumor was found in 5. Forty-two of the tumors were carcinomas and 5 were connective tissue tumors. In all but 2 cases the treatment consisted of deep x-ray therapy which was given by 2 methods. First, in the radiosensitive group in which cervical metastases, often bilateral, were the rule, regional treatment was the method of choice, i.e., an area from the base of the skull down to the clavicle was irradiated en bloc by two large lateral fields. The portal used in an adult was a 20 cm. circle to each side of the head and neck. The tumor dose given was between 3,000 and 3,500 roentgens in 4 to 5 weeks. The general reaction was usually marked so that the patient had to be hospitalized for the second half of the course of treatment. In the second group of patients, those with more highly differen-

tiated growths and without cervical metastases, intensive treatment was given by the use of 4 portals of entry of small size. A tumor dose between 5,500 and 6,000 roentgens in 6 to 7 weeks was given in these cases. When the glands were palpable in the second group, a compromise was struck. Regional irradiation with large fields was given up to a depth dose of 2,000 roentgens in 2 to 3 weeks, and then continued with small fields both to the primary tumor and the palpable cervical glands up to a tumor dose of 5,500 roentgens in 6 to 7 weeks. The factors employed were: 200-250 kv., 10 ma., Thoreus filter or filtration of 1 mm. of copper and 1 mm. of aluminum with a half-value layer of 2.4 or 1.4 mm. of copper, respectively. The focal skin distance was 40 cm. with small fields, and 60 cm. with 20 cm. circles. In this series 31 patients were given radical treatment 5 or more years ago. Of these, 8 survived without evidence of cancer for 5 or more years. Classified according to histology, the lymphoepithelioma and undifferentiated carcinoma showed the best 5-year results—2 of 5 and 4 of 11, respectively. In cases of differentiated squamous cell carcinoma and in transitional cell carcinoma the results were poor. Of the 3 patients with recticulum cell sarcoma, 2 died within the first year, while the third is alive and well 5.5 years later. The only patient with plasmocytoma in this series has survived, apparently free from growth, for 7 years. Invasion of the base of the skull carried a bad prognosis. Radiotherapy of this type of lesion must aim at eradication of the disease with the first course of treatment, as recurrences can hardly ever be cured.

FRANK L. HUSSEY, M.D.

Treatment of Cancer of the Breast. U. V. PORTMANN. *Radiology*, 1950, 55: 819.

The co-operative efforts of the physician, surgeon, radiologist, and pathologist are required in the treatment of carcinoma of the breast.

The decision as to whether a given case is curable or incurable is a primary problem. Surgery offers the only chance in those which are curable, yet it may hasten the growth in those beyond cure. It is, therefore, mandatory that the limitations of surgery and the indications for operation be recognized by all concerned.

The following clinical and pathological classification of carcinoma of the breast is given:

Group or stage I
- Skin: not involved
- Tumor: localized in the breast and movable
- Metastases: none in the axillary nodes or elsewhere

Group or stage II
- Skin: not involved
- Tumor: localized in the breast and movable
- Metastases: few axillary nodes involved; no metastases elsewhere

Group or stage III
- Skin: edematous. Brawny red induration or inflammation not obviously due to infection; extensive ulceration; multiple secondary nodules
- Tumor: diffusely infiltrating breast; fixation of tumor or breast to chest wall; edema of breast; secondary tumors
- Metastases: many axillary nodes involved or fixed. No clinical or roentgenologic evidences of remote metastases

Group or stage IV
- Skin: as in any other group or stage
- Tumor: as in any other group or stage
- Metastases: axillary and supraclavicular nodes extensively involved. Clinical or roentgenologic evidence of remote metastases.

Surgery alone will result in 5 year survival in 85 per cent of the cases in stage I. In the author's experience, postoperative roentgen therapy has not increased the survival rates in stage I.

In the cases in stage II, surgery alone yields a 5 year survival rate of less than 50 per cent. Postoperative x-ray therapy is indicated and will increase the 5 year survival from 10 to 15 per cent.

The average rate of 5 year survivals following operation alone is less than 15 per cent in stage III. A 10 per cent increase may be accomplished with postoperative roentgen therapy.

Surgery alone in stage IV, lesions without distant metastases, yields a 5 year survival of 5 per cent, which may be increased from 10 to 15 per cent by roentgen therapy. With distant metastases about 5 per cent of the patients may survive 5 years without therapy but irradiation will be palliative.

The author's criteria of incurability are presented as follows:

The skin
1. Edema (orange or pigskin) of more than slight extent
2. Ulceration of more than slight extent
3. Brawny red and inflamed, not obviously due to infection

The breast
1. Diffusely edematous
2. Diffusely infiltrated
3. Secondary tumors
4. Fixation of tumor or breast to chest wall

Metastases
1. Axillary lymph nodes—numerous, extensively involved, and fixed
2. Supraclavicular lymph nodes or edema of the arm
3. Involvement of contralateral breast or lymph nodes
4. Remote metastases in bones, lungs, or other viscera

Patients without criteria of incurability should be operated upon. If axillary nodes are found to be involved, roentgen therapy is indicated. Adequate radiation therapy will yield about a 15 per cent survival of patients with inoperable breast carcinoma. This is greater than the survival of those treated surgically and of those not treated. Roentgen sterilization is indicated in premenopausal patients with

criteria of incurability. Androgen and estrogen therapy is discussed briefly. JOHN WEIGEN, M.D.

Tissue Dose in Irradiation of the Breast. VINCENT P. COLLINS. *Radiology*, 1950, 55: 814.

Uniform tissue dosage can be obtained in irradiation of the breast by building the breast up with bolus material. A plastic box or frame with water-filled balloons adapts any breast to treatment with opposing, accurately directed, tangential beams.

The contour of the breast is determined and plotted by sighting through the transparent frame. Dosage may then be readily calculated by superimposing appropriate standard isodose curves. Experiments with phantoms show that such calculations are quite accurate when the breast is built up with bolus material, but that variations of 30 per cent above and below the predicted dose occur when bolus material is not used.

ALLAN K. BRINEY, M.D.

Radiation Therapy of Carcinoma of the Vagina. FRANZ BUSCHKE and SIMEON T. CANTRIL. *Radiology*, 1951, 56: 193.

Carcinoma of the vagina is rare. The proportion of vaginal carcinoma to carcinoma of the cervix is about 1 to 50. A clinically useful classification was proposed by Cantril, analogous to the staging of carcinoma of the cervix. He differentiates three stages:

Stage I. Nodular tumor or flat ulceration in surface area involving not more than one-half of either anterior or posterior vaginal wall, with only slight infiltration.

Stage II. Tumors with a surface area extending over more than half of the anterior or posterior vaginal wall, infiltrating paravaginal soft tissues unilaterally or bilaterally, and/or with moderate infiltration into the vesicovaginal or rectovaginal septum, but without fixation to pelvic bone and without demonstrable infiltration into the rectal (proctoscopy) or bladder mucosa (cystoscopy). The annular stenosing forms are included in this group.

Stage III. Tumors with infiltration, fixed to the pelvic bone or infiltrating mucosa of urethra, bladder, or rectum, or involving the vulva. A separate induration palpable in the pelvis apart from the primary lesion will place the case in the same category even if the primary lesion is less extensive. This Stage III would correspond to Stages III and IV of cancers of the cervix.

Ten cases of primary carcinoma of the vagina treated in the Tumor Institute of the Swedish Hospital, Seattle, Washington, during the period between 1942 and 1946 are presented. Six of these patients are well, without clinical signs of active disease, for periods of 3 to 6½ years. The treatment consisted of radical external roentgen therapy, complemented by local application of radiation. The importance of external irradiation in view of the rich lymphatic network of the vagina and the low degree of histologic differentiation of these tumors is emphasized. From an analysis of these cases and similar results obtained at the Institut du Radium (Paris), it is believed that the opinion of a particularly poor prognosis of carcinoma of the vagina is due to the insufficient external irradiation used in many instances.

FRANK L. HUSSEY, M.D.

Supraspinatus Tendinitis; A Survey of 300 Consecutive Cases Treated by Roentgen Therapy. OLIVER T. STEEN and J. A. L. MCCULLOUGH. *Am. J Roentg.*, 1951, 65: 245.

Supraspinatus tendinitis, which is the commonest cause of shoulder pain, was first considered to be a clinical entity by Codman and Painter. It is a disease of middle and later life, and therefore it is expected that its incidence will continue to increase coincident with our aging population.

The authors discuss the pathogenesis of the lesion at considerable length. It is assumed that the process starts at a "critical point" in the supraspinatus tendon near its insertion, where a relative local ischemia exists. Various factors, such as inefficient mechanics, attrition, occupational strain, and aging processes may provoke a degeneration of the tendon fibers in this region, resulting in avascular necrosis of varying degree. Following the initial phase of degeneration, a nonsuppurative foreign body reaction sets in, aiming at removal of the devitalized material. This inflammatory reaction then extends to the tendon sheath, the overlying bursa, and surrounding soft tissues, causing swelling with considerable pain and limitation of movement. The authors state that the lesion never arises primarily in the bursa. Soon fibrin formation occurs with further limitation of movement. With repeated subsequent episodes residual fibrosis develops, culminating in calcium deposition which is demonstrated in a considerable number of cases. The formation of the calcium deposit is explained on the theory of faulty oxidation in the devitalized tissues due to reduction in the formation of local CO_2 and consequent shift of the *p*H toward the alkaline side. This favors the precipitation of calcium salts, usually the carbonates and phosphates. The systemic calcium metabolism is unaltered.

The diagnosis is based on the severe pain in the shoulder, the limitation of movement which may be complete, and the roentgen visualization of calcium deposits. The authors stress that a roentgenologic examination is indicated in every case to determine the amount of the calcification present, and especially to rule out the possible presence of more serious lesions such as bone tumors.

Harrison described the following changes of the adjacent bone structures which may be observed on the roentgenograms: (1) irregularity of trabecular structure of cortical bone in the greater tuberosity; (2) minor erosions of articular cortex; (3) loss of normal contour of the anatomical humeral neck: (4) cystic cavitation at the tendon insertion; (5) areas of local bone sclerosis.

TABLE I.— RESULTS OF ROENTGEN THERAPY

	No. of cases	A Good result	B Fair result	A and B Favorable	C Slight effect	D No effect	C and D Records	
							Unfavorable	incompl. etc.
Entire series from Dep't records	300	139	112	251	13	25	38	11
	100%	46.3%	37.3%	83.6%	4.3%	8.3%	12.6%	3.7%
Series from questionnaire follow-up	171	94	57	151	0	20	20	0
	57%	56.7%	33.3%	89%	0	11%	11%	0
Patients who had other treatment	31	10	13	23	5	3	8	0
	10%	32%	41%	73%	17%	10%	17%	0
Patients with history of injury	76	39	26	65	4	4	8	3
	25.3%	51.3%	34.2%	85.5%	5.2%	5.2%	10.4%	4%
Patients with no history of injury	224	100	79	179	11	20	31	14
	70.4%	44.6%	35.2%	79.8%	4.9%	8.9%	13.8%	6.2%
Patients with roentgenographic calcium	152	72	57	129	4	14	18	5
	50.6%	48%	35%	83%	3%	9%	13%	4%
Patients without roentgenographic calcium	72	28	30	58	4	7	11	3
	24%	40%	41%	81%	5%	10%	15%	4%
Patients without roentgenographic examination	76	39	25	64	5	4	9	3
	24.4%	51%	33%	84%	6%	5%	11%	5%

The authors' material includes 300 patients who were treated by external roentgen therapy, with use of the following technique. A dose of 150 roentgens (in air) was given on four consecutive days, directed to the point of maximum tenderness through a 10 by 10 cm. port at 50 cm. skin target distance. The quality of the beam was that obtained with 200 kilovolts and filtered through 0.5 mm. plus 1 mm. of aluminum. In the majority of instances all symptoms subsided following a single course. In the more chronic cases, however, additional courses may be necessary at intervals of 1 month, and the daily dose may be raised to 200 roentgens (in air). The number of courses for the whole group was 1.5.

The results obtained are shown in Table I.

The conclusion is reached that roentgen therapy is a very useful method of management of nearly all cases of supraspinatus tendinitis. The presence of calcium deposits has no significant relationship to the therapeutic result and, therefore, it is of no prognostic value. Patients who had other types of treatment prior to roentgen therapy responded less favorably. T. LEUCUTIA, M.D.

Radiation-Induced, Squamous Cell Metaplasia and Hyperplasia of the Normal Mucous Glands of the Oral Cavity. MILTON FRIEDMAN and JOHN W. HALL. *Radiology*, 1950, 55: 848.

In a series of 64 patients studied at New York University, squamous cell metaplasia of the normal oral mucous glands was found rather frequently following radiotherapy for squamous cell carcinoma of the mouth and oropharynx. Through biopsies done before, during and following the completion of treatment, this change was picked up in 23 of 40 patients whose biopsy specimens contained mucous glands. The changes varied from case to case both in degree and in time of onset; in most cases they were mild, rarely marked. The sequence of events was: hypersecretion, inspissation of the secretion, atrophy of the acinar cells with decrease of the number of acini accompanied by replacement fibrosis, proliferation of the cells of the basal layers, finally various stages of squamous metaplasia, and, on rare occasions, hyperplasia of the metaplastic epithelium. In an occasional case, the proliferation was so marked that the picture might have been confused with well differentiated, infiltrating squamous cell carcinoma.

These findings are presented as another example of proliferative change induced by the irradiation of normal tissue; they are not considered a precancerous condition, and in no case did a cancer occur which could be related to the metaplasia.

WILLIAM C. OWSLEY, JR., M.D.

MISCELLANEOUS

Late Radiation Reaction in the Small Intestine Manifest 8 Years After Therapy; Report of a Case. RALPH C. FRANK and ERNST A. POHLE. *Ann. Surg.*, 1951, 133: 104.

Late radiation changes of the small intestine occur relatively seldom. This fact induced the authors to report a case showing such changes 8 years after roentgen therapy for advanced recurrent carcinoma of the colon. The outstanding clinical manifestation

was a low grade obstruction which was successfully relieved by operation, the patient having completely recovered.

The case, which is described in detail, is that of a 24 year old white female who, on barium enema examination in March, 1938, showed a large irregular filling defect in the ascending colon. Following several transfusions a right hemicolectomy with ileotransverse colostomy was done. Microscopic study revealed a highly anaplastic adenocarcinoma which had invaded the entire colonic wall and had produced metastases to the regional mesenteric lymph nodes.

In February, 1940 the patient returned with a recurrent mass in the cecal region for which a second operation was performed. The mass was found to be firmly attached to the anterior peritoneum with adhesions between it, the omentum, and the bowel. It was removed with some difficulty but apparently in its entirety. Exploration of the abdominal cavity revealed no gross evidence of further metastases.

In view of the fact that the microscopic examination of the recurrent tumor likewise showed a highly anaplastic adenocarcinoma, intensive postoperative irradiation was recommended. This was carried out by administering three successive series of roentgen therapy, the first from February 20 to March 1, 1940, with a dose of 9x200 roentgens (in air), the second from June 3 to June 11, 1940, with 8x200 roentgens (in air) and the third from January 13 to January 18, 1941 with 6x200 roentgens (in air) through 20 by 20 cm. ports to the anterior and posterior right abdomen. On each occasion roentgen rays obtained with 400 kilovolts were used, corresponding to a half value layer of 2.4 mm. copper, and the focus skin distance was 50 cm.

The patient enjoyed good health until the summer of 1948 when she developed vague symptoms of slowly progressing bowel obstruction. Within the next 6 months she was re-examined on several occasions and eventually a diagnosis of partial small bowel obstruction was made. The previously irradiated areas of the skin showed fibrosis, thickening, and telangiectasia, but no ulceration.

In January, 1949 a third operation was done, consisting of resection of a constricted segment of the terminal ileum, a generous portion of small bowel proximal to it, and a portion of the proximal transverse colon. Reanastomosis was established between the remaining ileum and the distal transverse colon. There was no evidence of recurrence of the former carcinoma.

The removed bowel which was approximately 28 cm. long exhibited typical late changes of radiation reaction.

In discussing the significance of these changes the authors refer to the work of Friedman and Warren who, in animal experiments, established the following sequence of the radiation effect on the intestine: (a) initial epithelial reaction which is more marked in the small bowel than the colon, (b) atrophy, (c) regeneration, which occurred more rapidly in the small intestine than in the colon, and (d) residua, consisting mainly of telangiectasia. Other investigators (Engelstad, Desjardins) made the observation that ulceration following irradiation is more apt to occur in the stomach and colon whereas the late changes in the small intestine are always characterized by telangiectasia, fibrosis, and stenosis. In the authors' case, inflammatory edema of the mucosa and submucosa also constituted an important part of the pathologic findings.

In concluding, the authors state that late radiation changes of the small intestine must be considered as unavoidable complications when the administration of a large effective dose is needed for the destruction of the cancer. As demonstrated in the reported case, the changes produced can be corrected without difficulty by skillful surgical intervention.

T. Leucutia, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

The Suprarenal Glands in Patients with Burns (Les surrénales des brulés). J. DELARUE, A. MONSAINGEON, and R. LAUMONIER. *Presse méd.*, 1950, 58: 1446.

The role of the suprarenal glands in the evolution of burns has been known for a long time, but the alterations in the glandular structure have never been well defined.

Recent progress in the treatment of burns offers opportunity to study advanced stages of extensive lesions to which, heretofore, patients would succumb soon after the accident. Moreover, the recognition of the alarm syndrome and the adaptation syndrome has integrated the clinical, histologic, and chemical modifications of the suprarenal glands and has demonstrated their role in the aforementioned nonspecific reactions of the organism.

The authors produced burns of various sizes in 13 rats and 14 rabbits by immersing them in hot water. The animals either died or were sacrificed at various intervals after the production of burns. In this manner it was possible to study chronologically the histologic changes in the suprarenal glands.

In early stages the spongiocytes lose their lipid contents. In rabbits such changes were noticed 2 hours after a severe burn. Retraction and increased density of the spongiocytes was noted in the fasciculi while the glomeruli remained intact. In rats similar changes were less pronounced as late as 8 hours after fatal burns because the resistance of rats is greater than that of rabbits. Alterations of the spongiocytes were delayed in rabbits with less severe burns.

The deficit in lipids is followed by their accumulation. The concomitant congestion and hypertrophy of the suprarenal cortex are responsible for the fact that the gland may attain a weight 8 times as great as that before the burn.

Histologic studies of the suprarenal glands in 9 patients who succumbed to burns from 1 to 78 days after the accident showed that similar changes take place in man. The degree of hypertrophy may not be identical in both glands of the same individual. Myeloid tissue may be found in the cortex, especially in deeply situated portions of the fasciculi, close to the reticulum. JOSEPH K. NARAT, M.D.

Influence of Dextran Ph on the Tensile Strength of Healing Wounds; An Experimental Study. GUNNAR THORSÉN. *Acta chir.*, scand., 1950, 100: 422.

The author showed in well controlled studies that infusions of therapeutic doses of Dextran Ph do not lower the tensile strength of experimentally produced wounds of rabbits during healing. This is ascribed primarily to the normal colloidal osmotic pressure that is maintained in spite of the relative anemia and hypoproteinemia produced by dextran. Apparently this colloid does not lower the contents of fibrinogen sufficiently to disturb the process of coagulation. Furthermore, as a result of the maintenance of the colloidal osmotic pressure at a normal level the development of edema is prevented, and firm and coarsely threaded fibrin clots are formed which encourage the formation of fibroblasts in spite of the hypoproteinemia.

The pertinent literature is discussed, and a bibliography is appended. ROBERT TURELL, M.D.

Epitheliomas of the Sweat Glands (Epiteliomas de las glándulas sudoríparas). N. PUENTE DUANY. *Arch. cuban. cancer.*, 1950, 9: 44.

This rather complete survey of sweat gland tumors divides the lesions into benign and malignant types, and lesions which develop from the hair follicles, the sebaceous glands, or from both. Some have hypoplastic characteristics throughout the whole tumor, whereas others are typical adenomas.

The malignant tumors are those of the basal cell group, clinically and histologically, as well as the anaplastic type with spindle cell or glandular characteristics. The difficulty in determining the type of epithelioma in some cases is recognized, but the importance of correct diagnosis cannot be minimized as the treatment to be established depends upon the benign or malignant character of the tumor.

The author divides the various tumors into six large groups, and with illustrations demonstrates the cellular features which point to a correct diagnosis.
STEPHEN A. ZIEMAN, M.D.

Carcinoma Occurring in the Sinuses of Chronic Osteomyelitis. K. L. MARKS and W. L. TURNER. *Brit. J. Surg.*, 1950, 38: 206.

Malignant change in chronic sinuses due to chronic osteomyelitis has long been known. The author states that the first case was reported by Hawkins, of London, in 1835. Fifty-two cases were reported up to 1931, and the writer lists 28 cases reported from then up to 1949. Three additional case reports are presented in this article. The condition occurred in 0.2508 per cent of the cases of chronic osteomyelitis reviewed by Henderson and Swart at the Mayo Clinic, and in 0.23 per cent of the series reported by McNally and Dockerty.

The condition occurs in males past middle age, the average age in the cases reported in this presentation being 51.6 years. The most common site is the femur. Diagnosis may be difficult and biopsy is necessary for confirmation. Enlargement of the regional glands occurs in two-thirds of the patients and is usually of inflammatory type. Radical amputation above the affected site is the treatment of choice. The prognosis is satisfactory after such treatment.
DONALD C. GEIST, M.D.

Cellular Transmission of Mouse Sarcomas with Frozen-Dried Tumor Tissues. L. DMOCHOWSKI and A. MILLARD. *Brit. M. J.*, 1950, 2: 1136.

To prove conclusively that frozen and desiccated tumor cells survive, the authors carried out the following experiment.

Suspensions of frozen and desiccated sarcoma cells embedded in clots formed by the addition of chick embryo extract to a mixture of rat and fowl plasmas were inoculated subcutaneously into mice. Sections of clots excised at varying intervals after grafting revealed the presence of viable tumor cells, increasing in numbers with the age of the grafts.

ELY ELLIOTT LAZARUS, M.D.

Mortality in Geriatric Surgery. LOUIS CARP. *Brit. M. J.*, 1950, 2: 1108.

The life span has shown a marked increase. In the United States, those aged 65 and over constitute 7.6 per cent of the population. With scientific advantages, improved techniques and anesthesia, and a better understanding of the degenerative processes accompanying old age, it has been possible for geriatric surgery to prolong life when it is threatened. The mortality rate in geriatric surgery in a large municipal hospital in the years 1945 through 1949 was 17 per cent, as compared to a mortality rate of 23 per cent during the period from 1939 to 1944.

In acute cases necessitating emergency surgery to reduce the mortality rate, there must be quick supportive therapy with the earliest and simplest operation to effect relief, and the institution of measures to prevent postoperative complications. The major causes of death in patients over 60 years of age who die within 1 month of operation are bronchopneumonia, heart failure, and peritonitis. The mortality rate in emergency surgery will be twice that of elective surgery.

ELY ELLIOTT LAZARUS, M.D.

EXPERIMENTAL SURGERY

Observations on the Growth of Aortic Anastomoses in Puppies. ELLIOTT S. HURWITT and SIGMUND A. BRAHMS. *Ann. Surg.*, 1951, 133: 200.

In coarctation of the aorta, the earlier the operation is done the better is the outcome. Attempts at reducing the time interval have been largely impeded by a lack of knowledge of the behavior of the anastomotic ring in terms of the subsequent growth of the aorta.

In order to determine whether or not the site of the anastomosis shares in the growth of the aorta, the authors operated on 18 puppies. The aorta was divided between the origin of the renal arteries and above the inferior mesenteric branch. Six of the animals survived long enough to permit unequivocal studies of the caliber of the anastomosis.

It was seen that there was a measurable increase of the caliber of the aorta, and the increase in the cross section area at the anastomosis was of the same relative order of magnitude as that for the normal aorta. The deformity created at the time of anastomosis persisted into adult life, resulting in a restricted lumen in this area. It was impossible to determine what proportion in size represented the actual growth and what was the result of stretch or distensibility.

It was concluded that these observations are not definitive enough to warrant a reduction in age for operation in coarctation of the aorta.

STEPHEN A. ZIEMAN, M.D.

The Therapeutic Effect of Aureomycin in Experimental Peritonitis in the Dog. FRITZ B. SCHWEINBURG, ALEXANDER M. RUTENBURG, SAMUEL MILROD, PHILIP GLOTZER, and JACOB FINE. *Ann. Surg.*, 1951, 133: 208.

Aureomycin was given to dogs to determine its effectiveness in experimental peritonitis. It was compared to sulfathalidine, streptomycin, and penicillin. It was found that when given orally it is most effective against the normal bacterial flora of the intestines. Coliform organisms and Clostridia are rapidly eliminated from the stools and gram-positive cocci are greatly reduced in numbers. Aureomycin is more effective for this purpose than sulfathalidine or streptomycin, singly or combined. It was stated that if a choice is to be made between streptomycin, penicillin, and aureomycin, the last should be preferred because the development of resistance to it is rare as compared to resistance to the other drugs.

STEPHEN A. ZIEMAN, M.D.

The Fascial Spaces of the Palm with Special Reference to Their Significance in Infections of the Hand. J. GARDNER JAMIESON. *Brit. J. Surg.*, 1950, 38: 193.

This article is concerned with the fascial spaces of the palm of the hand. It is based on a study of 59 hands in the Anatomical Department of the Medical College of St. Bartholomew's Hospital, London. In addition, 3 fresh specimens and 8 fixed cadaver hands were dissected and 48 hands were examined in the dissecting rooms to confirm points of detail. Previous studies of other workers and their findings are first discussed.

The palmar fascia is considered in detail. Emphasis is placed upon the anchoring fibers which extend dorsally and at right angles to the plane of the palm. There are 8 separate groups of these fibers forming a series of aponeurotic septa, one pair to each of the tendons of the four ulnar digits. The importance of these septa in Dupuytren's contracture is discussed.

The oblique septum is a thin sheet of connective tissue distinct from the septa described above. It splits to enclose the index tendons and first lumbrical muscle, a certain quantity of synovial-like fat, and portions of the digital and palmar serous sheaths of these tendons. Medially, the septum becomes indistinguishable from the fine membranous layer of the connective tissue forming the immediate roof of the middle palmar space.

The middle palmar space has as its medial wall the eighth aponeurotic septa and as its lateral wall the oblique septum. The floor is formed by the volar interosseus fascia over the third and fourth interosseus muscles and the fourth metacarpal bone. The roof is formed by the central part of the palmar aponeurosis. In it are the superficial and deep flexor tendons of the third, fourth and fifth digits, the second, third, and fourth lumbrical muscles, and the superficial vessels and nerves to the second, third, and fourth interdigital clefts. The adductor space has its medial wall formed by the oblique septum, and the lateral wall, by the muscles of the thenar eminence. The floor is formed by the epimysium on the volar surface of the adductor pollicis. The roof is formed by the palmar aponeurosis and extends between the radial longitudinal crease medially and the web of the thumb and summit of thenar eminence laterally.

The index tendon and first lumbrical muscle pass through the lateral border of the oblique septum and so occupy a common wall between the middle palmar and adductor spaces. Infection extending in the synovial sheath of the index tendon, therefore, might extend into either the middle palmar or adductor space. The same is true of infection spreading along the first lumbrical sheath.

No acceptable explanation for the oblique septum is found in the literature. It is now argued that it forms a retention band for the index tendons, having a definite functional role, and the subdivision of the palm is considered as secondary.

DONALD C. GEIST, M.D.

The Treatment of Cold Injury: Experimental Studies on the Extremities of Rabbits. The Effect of Prolonged Thawing and Warming.
STURE RÖDÉN. *Acta. chir.*, scand., 1950, 100: 515.

The author stated that the marked edema which is produced in frozen rabbit feet after thawing begins to appear at a skin temperature of about plus 23°C. It increases rapidly, but can be effectively checked by cooling the skin to below plus 20°C. When the cooling is stopped, the edema increases again. Whether the warming is rapid or slow from the minimum temperature up to plus 23 degrees does not seem to have any decisive effect on the starting rate of the edema or its final magnitude.

The consequences of the cold injury are more severe when the frozen part is thawed and warmed slowly than when warmed rapidly, although the edema is not as great when warmed slowly. The edema seems to be of less importance in the injury than the prolonged freezing. In 80 per cent of the experimental rabbits whose feet were thawed slowly, hemorrhagic edema, which is an indication of severe damage to the capillaries, was found.

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